

FOR OFFICIAL USE ONLY

ACCESS DB #

1646059

PLEASE PRINT CLEARLY

Scientific and Technical Information Center

SEARCH REQUEST FORM

Requester's Full Name: Sabika Qazi Examiner #: 74141 Date: 8/31/05
Art Unit: 0616 Phone Number: 2-0622 Serial Number: 109091928, 870
Location (Bldg/Room#): 4A45 (Mailbox #): 84C70 Results Format Preferred (circle) PAPER DISK

To ensure an efficient and quality search, please attach a copy of the cover sheet, claims, and abstract or fill out the following:

Title of Invention: Method of treatment of cancer by controlling graft-

Inventors (please provide full names): McDonald et al. Versus-Leukemia
using topical
active corticosteroid

Earliest Priority Date: 8/13/2001

Search Topic:

Please provide a detailed statement of the search topic, and describe as specifically as possible the subject matter to be searched. Include the elected species or structures, keywords, synonyms, acronyms, and registry numbers, and combine with the concept or utility of the invention. Define any terms that may have a special meaning. Give examples or relevant citations, authors, etc., if known.

For Sequence Searches Only Please include all pertinent information (parent, child, divisional, or issued patent numbers) along with the appropriate serial number.

Please search for the method of treating
a human patient ^{with cancer} by an steroid
betamethasone 17, 21-diproprionate to
reduce the mortality associated GVHD.
(Graft-v-Host Disease) as in cl 1.

Please see cl 15 where this compd is
used in combination of other drugs
additionally
you may search Medline, Biosis and
cancerlit.

Please see attached sheets.

Thank you.

=> d his ful

(FILE 'HOME' ENTERED AT 17:06:53 ON 14 SEP 2005)

FILE 'HCAPLUS' ENTERED AT 17:07:09 ON 14 SEP 2005

E MCDONALD GEORGE B/AU

L1 38 SEA ABB=ON "MCDONALD GEORGE B"/AU

E STERGIOPOULOS NICHOLAS/AU

L2 4 SEA ABB=ON "STERGIOPOULOS NICHOLAS"/AU

L3 2 SEA ABB=ON L1 AND L2

L4 ANALYZE L3 1-2 CT : 15 TERMS

FILE 'REGISTRY' ENTERED AT 17:33:22 ON 14 SEP 2005

L5 5 SEA ABB=ON (PREDNISONE OR PREDNISOLONE OR CYCLOSPORINE OR

METHOTREXATE OR TACROLIMUS) /CN

E ANTI-LYMPHOCYTE GLOBULIN/CN

E GLOBULIN ANTI-LYMPHOCYTE/CN

E GLOBULIN, ANTI-LYMPHOCYTE/CN

E ANTI-T-CELL MONOCLONAL ANTIBODIES/CN

L6 1 SEA ABB=ON BECLOMETHASONE 17,21-DIPROPIONATE/CN

FILE 'HCAPLUS' ENTERED AT 17:35:00 ON 14 SEP 2005

L7 1030 SEA ABB=ON (?HEMATOPOIETIC? (3W)?CELL? (3A)?TRANSPLANT?)

L8 173 SEA ABB=ON L7 AND (?GVHD? OR ?GRAFT? (W)V(W)?HOST? (W)?DISEASE?)

L9 1 SEA ABB=ON L8 AND GVL(W)?REACT?

L10 67 SEA ABB=ON L8 AND (?CANCER? OR ?CARCIN? OR ?NEOPLASM? OR
?TUMOR? OR ?TUMOUR?)

L11 1 SEA ABB=ON L10 AND (L6 OR ?BECLOMETHASONE-17,21-DIPROPIONAT?)

L12 26 SEA ABB=ON L10 AND (L5 OR ?PREDNISONE? OR ?PREDNISOLONE? OR
?CYCLOSPORINE? OR ?METHOTREXATE? OR ?ANTI? (W)?LYMPHOCYTE? (W)?GLO
BULIN? OR ?ANTI? (W)T(W)?CELL? (W)(MONOCLONAL? (W)?ANTIBOD? OR
?IMMUNOTOXIN?))

L13 26 SEA ABB=ON L11 OR L12

L14 6 SEA ABB=ON L13 AND (PRD<20010813 OR PD<20010813) *6 cits from CA Plus*

FILE 'MEDLINE, CANCERLIT, BIOSIS, EMBASE, JAPIO, JICST-EPLUS' ENTERED AT
17:42:24 ON 14 SEP 2005

L15 24 SEA ABB=ON L13

L16 16 DUP REMOV L15 (8 DUPLICATES REMOVED) *16 cits from above db's*

FILE 'USPATFULL' ENTERED AT 17:46:17 ON 14 SEP 2005

L17 15 SEA ABB=ON L13 AND (PRD<20010813 OR PD<20010813) *15 cits from USPatfull*

L18 0 SEA ABB=ON L17 AND (L6 OR ?BECLOMETHASONE?-17,21-?DIPROPIONAT?)

FILE 'MEDLINE, CANCERLIT, BIOSIS, EMBASE, JAPIO, JICST-EPLUS' ENTERED AT
17:47:18 ON 14 SEP 2005

L19 0 SEA ABB=ON L16 AND (L6 OR ?BECLOMETHASONE-17,21-DIPROPIONAT?)

FILE 'HCAPLUS' ENTERED AT 17:48:02 ON 14 SEP 2005

L20 1 SEA ABB=ON L10 AND ?BECLOMETHASONE?

FILE 'MEDLINE, CANCERLIT, BIOSIS, EMBASE, JAPIO, JICST-EPLUS' ENTERED AT
17:48:24 ON 14 SEP 2005

L21 0 SEA ABB=ON L16 AND ?BECLOMETHASONE?

FILE 'USPATFULL' ENTERED AT 17:48:46 ON 14 SEP 2005

L22 0 SEA ABB=ON L17 AND ?BECLOMETHASONE?

FILE HOME

FILE HCAPLUS

Copyright of the articles to which records in this database refer is held by the publishers listed in the PUBLISHER (PB) field (available for records published or updated in Chemical Abstracts after December 26, 1996), unless otherwise indicated in the original publications. The CA Lexicon is the copyrighted intellectual property of the American Chemical Society and is provided to assist you in searching databases on STN. Any dissemination, distribution, copying, or storing of this information, without the prior written consent of CAS, is strictly prohibited.

FILE COVERS 1907 - 14 Sep 2005 VOL 143 ISS 12
FILE LAST UPDATED: 13 Sep 2005 (20050913/ED)

New CAS Information Use Policies, enter HELP USAGETERMS for details.

This file contains CAS Registry Numbers for easy and accurate substance identification.

FILE REGISTRY

Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

STRUCTURE FILE UPDATES: 13 SEP 2005 HIGHEST RN 863091-33-2
DICTIONARY FILE UPDATES: 13 SEP 2005 HIGHEST RN 863091-33-2

New CAS Information Use Policies, enter HELP USAGETERMS for details.

TSCA INFORMATION NOW CURRENT THROUGH JULY 14, 2005

Please note that search-term pricing does apply when conducting SmartSELECT searches.

*
* The CA roles and document type information have been removed from *
* the IDE default display format and the ED field has been added, *
* effective March 20, 2005. A new display format, IDERL, is now *
* available and contains the CA role and document type information. *
*

Structure search iteration limits have been increased. See HELP SLIMITS for details.

Experimental and calculated property data are now available. For more information enter HELP PROP at an arrow prompt in the file or refer to the file summary sheet on the web at:
<http://www.cas.org/ONLINE/DBSS/registryss.html>

FILE MEDLINE

FILE LAST UPDATED: 14 SEP 2005 (20050914/UP). FILE COVERS 1950 TO DATE.

On December 19, 2004, the 2005 MeSH terms were loaded.

The MEDLINE reload for 2005 is now available. For details enter HELP RLOAD at an arrow prompt (=>). See also:

<http://www.nlm.nih.gov/mesh/>
http://www.nlm.nih.gov/pubs/techbull/nd04/nd04_mesh.html

OLDMEDLINE now back to 1950.

MEDLINE thesauri in the /CN, /CT, and /MN fields incorporate the MeSH 2005 vocabulary.

This file contains CAS Registry Numbers for easy and accurate substance identification.

FILE CANCERLIT

FILE COVERS 1963 TO 15 Nov 2002 (20021115/ED)

On July 28, 2002, CANCERLIT was reloaded. See HELP RLOAD for details.

CANCERLIT thesauri in the /CN, /CT, and /MN fields incorporate the MeSH 2002 vocabulary. Enter HELP THESAURUS for details.

This file contains CAS Registry Numbers for easy and accurate substance identification.

FILE BIOSIS

FILE COVERS 1969 TO DATE.

CAS REGISTRY NUMBERS AND CHEMICAL NAMES (CNS) PRESENT
FROM JANUARY 1969 TO DATE.

RECORDS LAST ADDED: 8 September 2005 (20050908/ED)

FILE RELOADED: 19 October 2003.

FILE EMBASE

FILE COVERS 1974 TO 9 Sep 2005 (20050909/ED)

EMBASE has been reloaded. Enter HELP RLOAD for details.

This file contains CAS Registry Numbers for easy and accurate substance identification.

FILE JAPIO

FILE LAST UPDATED: 5 SEP 2005 <20050905/UP>

FILE COVERS APR 1973 TO APRIL 28, 2005

<<< GRAPHIC IMAGES AVAILABLE >>>

FILE JICST-EPLUS

FILE COVERS 1985 TO 13 SEP 2005 (20050913/ED)

THE JICST-EPLUS FILE HAS BEEN RELOADED TO REFLECT THE 1999 CONTROLLED TERM (/CT) THESAURUS RELOAD.

FILE USPATFULL

FILE COVERS 1971 TO PATENT PUBLICATION DATE: 13 Sep 2005 (20050913/PD)

FILE LAST UPDATED: 13 Sep 2005 (20050913/ED)

HIGHEST GRANTED PATENT NUMBER: US6944881

HIGHEST APPLICATION PUBLICATION NUMBER: US2005198721

CA INDEXING IS CURRENT THROUGH 13 Sep 2005 (20050913/UPCA)
ISSUE CLASS FIELDS (/INCL) CURRENT THROUGH: 13 Sep 2005 (20050913/PD)
REVISED CLASS FIELDS (/NCL) LAST RELOADED: Jun 2005
USPTO MANUAL OF CLASSIFICATIONS THESAURUS ISSUE DATE: Jun 2005

>>> USPAT2 is now available. USPATFULL contains full text of the <<<
>>> original, i.e., the earliest published granted patents or <<<
>>> applications. USPAT2 contains full text of the latest US <<<
>>> publications, starting in 2001, for the inventions covered in <<<
>>> USPATFULL. A USPATFULL record contains not only the original <<<
>>> published document but also a list of any subsequent <<<
>>> publications. The publication number, patent kind code, and <<<
>>> publication date for all the US publications for an invention <<<
>>> are displayed in the PI (Patent Information) field of USPATFULL <<<
>>> records and may be searched in standard search fields, e.g., /PN, <<<
>>> /PK, etc. <<<

>>> USPATFULL and USPAT2 can be accessed and searched together <<<
>>> through the new cluster USPATALL. Type FILE USPATALL to <<<
>>> enter this cluster. <<<

>>> Use USPATALL when searching terms such as patent assignees, <<<
>>> classifications, or claims, that may potentially change from <<<
>>> the earliest to the latest publication. <<<

This file contains CAS Registry Numbers for easy and accurate substance identification.

Inventor Search

Qazi 09/913,435

14/09/2005

=> d ibib abs ind 13 1-2

L3 ANSWER 1 OF 2 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2003:118593 HCAPLUS

DOCUMENT NUMBER: 138:148132

TITLE: Method of treatment of cancer by controlling
graft-versus-leukemia using topical active
corticosteroids

INVENTOR(S): McDonald, George B.; Stergiopoulos,

Nicholas

PATENT ASSIGNEE(S): USA

SOURCE: U.S. Pat. Appl. Publ., 5 pp.

CODEN: USXXCO

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
-----	-----	-----	-----	-----
US 2003032631	A1	20030213	US 2001-928890	20010813
PRIORITY APPLN. INFO.:			US 2001-928890	20010813

AB A method for the improved treatment of blood-borne cancers, such as lymphomas, leukemia, and myeloma is disclosed. The method comprises the oral administration of an effective amount of a topically active corticosteroid (TAC) to a patient who has undergone hematopoietic cell transplantation. Administration of the TAC controls a graft-vs.-leukemia (GVL) reaction that is induced following a hematopoietic cell transplantation, so that a GVHD reaction does not develop, or is reduced in severity. The GVL reaction effects killing of cancerous tumor cells in the blood, mediated by the cells derived from the hematopoietic cell transplantation.

IC ICM A61K031-56

INCL 514178000; 514179000; 514180000

CC 2-4 (Mammalian Hormones)

ST leukemia treatment cancer corticosteroid host versus graft allotransplant

IT Antibodies and Immunoglobulins

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(antilymphocyte globulins, in combination with corticosteroids; methods and combinations for the treatment of cancer by controlling graft-vs.-leukemia using topical active corticosteroids)

IT Neoplasm

(blood-born; methods and combinations for the treatment of cancer by controlling graft-vs.-leukemia using topical active corticosteroids)

IT Transplant and Transplantation

(graft-vs.-host reaction, prevention and reduction of symptoms; methods and combinations for the treatment of cancer by controlling graft-vs.-leukemia using topical active corticosteroids)

IT Transplant and Transplantation

(hematopoietic cells; methods and combinations for the treatment of cancer by controlling graft-vs.-leukemia using topical active corticosteroids)

IT T cell (lymphocyte)

(immunotoxins and antibodies against; methods and combinations for the treatment of cancer by controlling graft-vs.-leukemia using topical active corticosteroids)

IT Drug delivery systems

(immunotoxins, anti-T-cells, in combination with corticosteroids;

methods and combinations for the treatment of cancer by controlling graft-vs.-leukemia using topical active corticosteroids)

IT Antitumor agents
 Human
 Leukemia
 Lymphoma
 Multiple myeloma
 (methods and combinations for the treatment of cancer by controlling graft-vs.-leukemia using topical active corticosteroids)

IT Corticosteroids, biological studies
 RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (methods and combinations for the treatment of cancer by controlling graft-vs.-leukemia using topical active corticosteroids)

IT Antibodies and Immunoglobulins
 RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (monoclonal, anti-T-cells, in combination with corticosteroids; methods and combinations for the treatment of cancer by controlling graft-vs.-leukemia using topical active corticosteroids)

IT 50-24-8, Prednisolone 53-03-2, Prednisone 59-05-2, Methotrexate 59865-13-3, Cyclosporine 104987-11-3, Tacrolimus
 RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (in combination with corticosteroids; methods and combinations for the treatment of cancer by controlling graft-vs.-leukemia using topical active corticosteroids)

IT 76-25-5 1524-88-5, Flurandrenolide 3093-35-4, Halcinonide 3385-03-3, Flunisolide 5534-09-8, Beclomethasone 17,21-dipropionate 5534-18-9, Beclomethasone-17-monopropionate 25122-46-7, Clobetasol propionate 33564-31-7, Diflorasone diacetate 51333-22-3, Budesonide 51372-28-2 51372-29-3 66734-13-2, Alclometasone dipropionate 66852-54-8, Halobetasol propionate 80474-14-2, Fluticasone propionate 83919-23-7, Mometasone furoate
 RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (methods and combinations for the treatment of cancer by controlling graft-vs.-leukemia using topical active corticosteroids)

L3 ANSWER 2 OF 2 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2002:505407 HCAPLUS
 DOCUMENT NUMBER: 137:42096
 TITLE: Method of long-term treatment of graft-versus-host disease using topical active corticosteroids
 INVENTOR(S): McDonald, George B.; Stergiopoulos, Nicholas
 PATENT ASSIGNEE(S): USA
 SOURCE: U.S. Pat. Appl. Publ., 4 pp.
 CODEN: USXXCO
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
-----	-----	-----	-----	-----
US 2002086857	A1	20020704	US 2001-753814	20010103
US 2004006053	A1	20040108	US 2003-613788	20030703
PRIORITY APPLN. INFO.:			US 2000-233194P	P 20000915

US 2001-753814 B1 20010103

- AB A method for long-term therapy using corticosteroids to treat tissue damage associated with graft-vs.-host disease in a patient having undergone hematopoietic cell transplantation, and host-vs.-graft disease in a patient having undergone organ allograft transplantation. The method includes orally administering to the patient a therapeutically effective amount of a topically active corticosteroid, such as beclomethasone dipropionate, from the 29th day until the 56th day following hematopoietic cell or organ allograft transplantation. Representative tissues includes tissue of the intestine and liver, while representative tissue damage includes inflammation thereof.
- IC ICM A61K031-573
- INCL 514179000
- CC 2-4 (Mammalian Hormones)
Section cross-reference(s): 15
- ST graft vs host disease treatment corticosteroid
- IT Transplant and Transplantation
(allograft; method of long-term treatment of tissue damage caused by graft-vs.-host disease using topical active corticosteroids)
- IT Transplant and Transplantation
(graft-vs.-host reaction; method of long-term treatment of tissue damage caused by graft-vs.-host disease using topical active corticosteroids)
- IT Transplant and Transplantation
(hematopoietic cell transplantation; method of long-term treatment of tissue damage caused by graft-vs.-host disease using topical active corticosteroids)
- IT Human
Inflammation
Intestine, disease
Liver, disease
(method of long-term treatment of tissue damage caused by graft-vs.-host disease using topical active corticosteroids)
- IT Corticosteroids, biological studies
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(method of long-term treatment of tissue damage caused by graft-vs.-host disease using topical active corticosteroids)
- IT Hematopoietic precursor cell
(transplant; method of long-term treatment of tissue damage caused by graft-vs.-host disease using topical active corticosteroids)
- IT 50-24-8, Prednisolone 53-03-2, Prednisone 76-25-5, Triamcinolone acetonide 1524-88-5, Flurandrenolide 3093-35-4, Halcinonide 3385-03-3, Flunisolide 5534-09-8, Beclomethasone dipropionate 5534-18-9, Beclomethasone-17-monopropionate 25122-46-7, Clobetasol propionate 33564-31-7, Diflorasone diacetate 51333-22-3, Budesonide 51372-28-2 51372-29-3 66734-13-2, Alclometasone dipropionate 66852-54-8, Halobetasol propionate 80474-14-2, Fluticasone propionate 83919-23-7, Mometasone furoate
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(method of long-term treatment of tissue damage caused by graft-vs.-host disease using topical active corticosteroids)

```
=> d que stat 114
L5      5 SEA FILE=REGISTRY ABB=ON (PREDNISONE OR PREDNISOLONE OR
CYCLOSPORINE OR METHOTREXATE OR TACROLIMUS)/CN
L6      1 SEA FILE=REGISTRY ABB=ON BECLOMETHASONE 17,21-DIPROPIONATE/CN
L7      1030 SEA FILE=HCAPLUS ABB=ON (?HEMATOPOIETIC?(3W)?CELL?(3A)?TRANSPL
ANT)
L8      173 SEA FILE=HCAPLUS ABB=ON L7 AND (?GVHD? OR ?GRAFT?(W)V(W)?HOST?
(W)?DISEASE?)
L10     67 SEA FILE=HCAPLUS ABB=ON L8 AND (?CANCER? OR ?CARCIN? OR
?NEOPLASM? OR ?TUMOR? OR ?TUMOUR?)
L11     1 SEA FILE=HCAPLUS ABB=ON L10 AND (L6 OR ?BECLOMETHASONE-17,21-D
IPROPIONAT?)
L12     26 SEA FILE=HCAPLUS ABB=ON L10 AND (L5 OR ?PREDNISONE? OR
?PREDNISOLONE? OR ?CYCLOSPORINE? OR ?METHOTREXAT? OR ?ANTI?(W)?
LYMPHOCYTE?(W)?GLOBULIN? OR ?ANTI?(W)T(W)?CELL?(W)(MONOCLONAL?(W)?
W)?ANTIBOD? OR ?IMMUNOTOXIN?))
L13     26 SEA FILE=HCAPLUS ABB=ON L11 OR L12
L14     6 SEA FILE=HCAPLUS ABB=ON L13 AND (PRD<20010813 OR PD<20010813)
```

=> d ibib abs 114 1-6

L14 ANSWER 1 OF 6 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2001:917046 HCAPLUS
DOCUMENT NUMBER: 136:193827
TITLE: Nonablative allogeneic hematopoietic transplantation
as adoptive immunotherapy for indolent lymphoma: low
incidence of toxicity, acute graft-versus-host
disease, and treatment-related mortality
AUTHOR(S): Khouri, Issa F.; Saliba, Rima M.; Giralt, Sergio A.;
Lee, Ming-Sheng; Okoroji, Grace-Julia; Hagemeister,
Fredrick B.; Korbling, Martin; Younes, Anas; Ippoliti,
Cindy; Gajewski, James L.; McLaughlin, Peter;
Anderlini, Paolo; Donato, Michele L.; Cabanillas,
Fernando F.; Champlin, Richard E.
CORPORATE SOURCE: Departments of Blood and Marrow Transplantation,
Lymphoma, Laboratory Medicine, University of Texas M.
D. Anderson Cancer Center, Houston, TX, 77030, USA
SOURCE: Blood (2001), 98(13), 3595-3599
CODEN: BLOOAW; ISSN: 0006-4971
PUBLISHER: American Society of Hematology
DOCUMENT TYPE: Journal
LANGUAGE: English

AB This study investigated the use of a nonablative conditioning regimen to decrease toxicity and achieve engraftment of an allogeneic blood stem cell transplant, allowing a graft-vs.-malignancy effect to occur. All patients had follicular or small cell lymphocytic lymphoma after relapse from a prior response to conventional chemotherapy. Patients received a preparative regimen of fludarabine (25 mg/m² given daily for 5 days or 30 mg/m² daily for 3 days) and i.v. cyclophosphamide (1 g/m² given daily for 2 days or 750 mg/m² daily for 3 days). Nine patients received rituximab in addition to the chemotherapy. Tacrolimus and methotrexate were used for graft-vs.-host disease (**GVHD**) prophylaxis. Twenty patients were studied; their median age was 51 yr. Twelve were in complete remission (CR) at transplantation. All patients achieved engraftment of donor cells. The median number of days with severe neutropenia was 6. Only 2 patients required more than one platelet transfusion. The cumulative incidence of acute grade II to IV **GVHD** was 20%. Only one patient developed acute **GVHD** of greater than grade II. All patients achieved CR. None have had a relapse

of disease, with a median follow-up period of 21 mo. The actuarial probability of being alive and in remission at 2 yr was 84% (95% confidence interval, 57%-94%). Nonablative chemotherapy with fludarabine/cyclophosphamide followed by allogeneic stem cell transplantation is a promising therapy for indolent lymphoma with minimal toxicity and myelosuppression. Further studies are warranted to compare nonablative allogeneic hematopoietic transplantation with alternative treatment strategies.

REFERENCE COUNT: 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 2 OF 6 HCPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2001:549793 HCPLUS

DOCUMENT NUMBER: 135:327107

TITLE: Nonmyeloablative hematopoietic cell transplantation:
Replacing high-dose cytotoxic therapy by the
graft-versus-**tumor** effect

AUTHOR(S): Feinstein, Lyle; Sandmaier, Brenda; Maloney, David;
McSweeney, Peter A.; Maris, Michael; Flowers,
Christopher; Radich, Jerry; Little, Marie-Terese;
Nash, Richard A.; Chauncey, Thomas; Woolfrey, Ann;
Georges, George; Kiem, Hans-Peter; Zaucha, Jan M.;
Blume, Karl G.; Shizuru, Judith; Niederwieser,
Dietger; Storb, Rainer

CORPORATE SOURCE: Fred Hutchinson Cancer Research Center, Seattle, WA,
98109-1024, USA

SOURCE: Annals of the New York Academy of Sciences (2001), 938(Hematopoietic Stem Cells 2000),
328-339

CODEN: ANYAA9; ISSN: 0077-8923
PUBLISHER: New York Academy of Sciences

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Conventional allografting produces considerable regimen-related toxicities that generally limit this treatment to patients younger than 55 yr and in otherwise good medical condition. T cell-mediated graft-vs.-**tumor** (GVT) effects are known to play an important role in the elimination of malignant disease after allotransplants. A minimally myelosuppressive regimen that relies on immunosuppression for allogeneic engraftment was developed to reduce toxicities while optimizing GVT effects. Pre-transplant total-body irradiation (200 cGy) followed by post-transplant immunosuppression with **cyclosporine** (CSP) and mycophenolate mofetil (MMF) permitted human leukocyte antigen (HLA)-matched sibling donor hematopoietic cell engraftment in 82% of patients (n = 55) without prior high-dose therapy. The addition of fludarabine (90 mg/M2) facilitated engraftment in all 28 subsequent patients. Overall, fatal progression of underlying disease occurred in 20% of patients after transplant. Non-relapse mortality occurred in 11% of patients. Toxicities were low. Grade 2-4 acute graft-vs.-host disease (**GVHD**) associated with primary engraftment developed in 47% of patients, and was readily controlled in all but two patients. Donor lymphocyte infusions (DLI) were not very effective at converting a low degree of mixed donor/host chimerism to full donor chimerism; however, the addition of fludarabine reduced the need for DLI. With a median follow-up of 244 days, 68% of patients were alive, with 42% of patients in complete remission, including mol. remissions. Remissions occurred gradually over periods of weeks to a year. If long-term efficacy is demonstrated, such a strategy would expand treatment options for patients who would otherwise be excluded from conventional allografting.

REFERENCE COUNT: 59 THERE ARE 59 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 3 OF 6 HCAPLUS COPYRIGHT 2005 ACS on STN
 ACCESSION NUMBER: 2001:417759 HCAPLUS
 DOCUMENT NUMBER: 135:162240
 TITLE: Hematopoietic cell transplantation in older patients with hematologic malignancies: replacing high-dose cytotoxic therapy with graft-versus-tumor effects
 AUTHOR(S): McSweeney, Peter A.; Niederwieser, Dietger; Shizuru, Judith A.; Sandmaier, Brenda M.; Molina, Arthur J.; Malone, David G.; Chauncey, Thomas R.; Gooley, Theodore A.; Hegenbart, Ute; Nash, Richard A.; Radich, Jerald; Wagner, John L.; Minor, Steven; Appelbaum, Frederick R.; Bensinger, William I.; Bryant, Eileen; Flowers, Mary E. D.; Georges, George E.; Grumet, F. Cart; Kiem, Hans-Peter; Torok-Storb, Beverly; Yu, Cong; Blume, Karl G.; Storb, Rainer F.
 CORPORATE SOURCE: Fred Hutchinson Cancer Research Center, University of Washington School of Medicine, Seattle, WA, USA
 SOURCE: Blood (2001), 97(11), 3390-3400
 CODEN: BLOOAW; ISSN: 0006-4971
 PUBLISHER: American Society of Hematology
 DOCUMENT TYPE: Journal
 LANGUAGE: English

AB Toxicities have limited the use of allogeneic hematopoietic cell transplantation (HCT) to younger, medically fit patients. In a canine HCT model, a combination of postgrafting mycophenolate mofetil (MMF) and cyclosporine (CSP) allowed stable allogeneic engraftment after minimally toxic conditioning with low-dose (200 cGy) total-body irradiation (TBI). These findings, together with the known antitumor effects of donor leukocyte infusions (DLIs), led to the design of this trial. Forty-five patients (median age 56 yr) with hematol. malignancies, HLA-identical sibling donors, and relative contraindications to conventional HCT were treated. Immunosuppression involved TBI of 200 cGy before and CSP/MMF after HCT. DLIs were given after HCT for persistent malignancy, mixed chimerism, or both. Regimen toxicities and myelosuppression were mild, allowing 53% of eligible patients to have entirely outpatient transplantations. Nonfatal graft rejection occurred in 20% of patients. Grades II to III acute graft-vs.-host disease (GVHD) occurred in 47% of patients with sustained engraftment. With median follow-up of 417 days, survival was 66.7%, nonrelapse mortality 6.7%, and relapse mortality 26.7%. Fifty-three percent of patients with sustained engraftment were in complete remission, including 8 with mol. remissions. This novel allografting approach, based on the use of post-grafting immunosuppression to control graft rejection and GVHD, has dramatically reduced the acute toxicities of allografting. HCT with the induction of potent graft-vs.-tumor effects can be performed in previously ineligible patients, largely in an outpatient setting. Future protocol modifications should reduce rejection and GVHD, thereby facilitating studies of allogeneic immunotherapy for a variety of malignancies.

REFERENCE COUNT: 62 THERE ARE 62 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 4 OF 6 HCAPLUS COPYRIGHT 2005 ACS on STN
 ACCESSION NUMBER: 1999:427885 HCAPLUS
 DOCUMENT NUMBER: 131:97039

TITLE: A new preconditioning regimen with melphalan, busulphan and total body irradiation followed by low-dose immunosuppressant in allogeneic hemopoietic stem cell transplantation

AUTHOR(S): Murata, Makoto; Nishida, Tetsuya; Haneda, Masataka; Kanie, Tadaharu; Taji, Hirofumi; Iida, Hiroatsu; Suzuki, Ritsuro; Hamaguchi, Motohiro; Minami, Saburo; Kodera, Yoshihisa

CORPORATE SOURCE: Department of Internal Medicine, Japanese Red Cross Nagoya First Hospital, Nagoya, 453-8511, Japan

SOURCE: British Journal of Haematology (1999), 105(3), 799-802

CODEN: BJHEAL; ISSN: 0007-1048

PUBLISHER: Blackwell Science Ltd.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Twenty adult patients with high-risk leukemia underwent allogeneic hemopoietic stem cell transplantation after melphalan, busulfan and total body irradiation followed by short-term **methotrexate** and low-dose **cyclosporine** or tacrolimus. Three patients developed veno-occlusive disease and no patient developed renal dysfunction. Seven patients experienced grade II-IV acute graft-vs.-host disease (**aGVHD**) and five patients experienced grade III-IV. The 3-yr probabilities of relapse and leukemia-free survival were 22±11% (95% confidence interval) and 50±11%, resp. These data suggest that this preconditioning regimen followed by a low-dose immunosuppressant provided a more anti-leukemic effect without increased regimen-related toxicity and **aGVHD**.

REFERENCE COUNT: 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 5 OF 6 HCPLUS COPYRIGHT 2005 ACS on STN
 ACCESSION NUMBER: 1999:409973 HCPLUS
 DOCUMENT NUMBER: 131:82719

TITLE: Total body irradiation, thiotaepa, and cyclophosphamide as a conditioning regimen for children with acute lymphoblastic leukemia in first or second remission undergoing bone marrow transplantation with HLA-identical siblings

AUTHOR(S): Zecca, Marco; Pession, Andrea; Messina, Chiara; Bonetti, Federico; Favre, Claudio; Prete, Arcangelo; Cesaro, Simone; Porta, Fulvio; Mazzarino, Ida; Giorgiani, Giovanna; Rondelli, Roberto; Locatelli, Franco

CORPORATE SOURCE: Department of Pediatrics, University of Pavia, IRCCS Policlinico San Matteo, Pavia, I-27100, Italy

SOURCE: Journal of Clinical Oncology (1999), 17(6), 1838-1846

CODEN: JCONDN; ISSN: 0732-183X

PUBLISHER: Lippincott Williams & Wilkins

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Purpose: Allogeneic hematopoietic stem-cell transplantation (HSCT) from HLA-identical siblings can be used to treat children with acute lymphoblastic leukemia (ALL). However, a significant proportion of patients with ALL who undergo HSCT relapse. For this reason, we prospectively evaluated a preparative regimen that included total body irradiation (TBI), thiotaepa (TT), and cyclophosphamide (CY) in patients with high-risk ALL in first complete remission (CR) and in children with ALL in

second CR. Patients and Methods: Forty children (median age, 9 yr; range, 1 to 18 yr) with ALL in first or second CR who underwent allogeneic HSCT from HLA-identical siblings were conditioned with a combination of fractionated TBI, TT (10 mg/kg), and CY (120 mg/kg over 2 days). Graft-vs.-host disease (**GVHD**) prophylaxis consisted of **cyclosporine** administered i.v. at a dose of 1 to 3 mg/kg/d for the first 21 days and subsequently orally at a dose of 6 mg/kg/d. Results: All assessable patients were engrafted, with a median time of 11 and 24 days for neutrophil and platelet recovery, resp. The preparative regimen was well tolerated. Only one patient died as a result of regimen-related causes. Eight patients relapsed at a median time of 8 mo after transplantation (range, 3 to 9 mo), and this determined a cumulative probability of relapse of 23%. Twenty-six of 40 patients (65%) are alive and in complete hematol. remission, with a median observation time of 36 mo (range, 14 to 57 mo), which results in a disease-free survival (DFS) at 3 yr of 65%. The 13 patients who underwent transplantation in first CR had a DFS of 85%, whereas the 27 patients who underwent HSCT in second CR had a DFS of 56%. Conclusion: These data suggest that TT is an effective cytotoxic drug that can be safely added to the classical TBI-CY regimen. Because of its cell cycle-independent action, good CNS diffusion, and limited extramedullary toxicity, TT may contribute to increasing the percentage of children with ALL who are successfully cured with allogeneic BMT.

REFERENCE COUNT: 52 THERE ARE 52 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 6 OF 6 HCPLUS COPYRIGHT 2005 ACS on STN
 ACCESSION NUMBER: 1999:344857 HCPLUS
 DOCUMENT NUMBER: 131:4246
 TITLE: Treatment of hematologic disorders
 INVENTOR(S): Sykes, Megan; Spitzer, Thomas R.
 PATENT ASSIGNEE(S): The General Hospital Corporation, USA
 SOURCE: PCT Int. Appl., 60 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9925367	A2	19990527	WO 1998-US24209	19981113 <--
WO 9925367	A3	19990805		
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2309919	AA	19990527	CA 1998-2309919	19981113 <--
EP 1030675	A2	20000830	EP 1998-960199	19981113 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
JP 2001523645	T2	20011127	JP 2000-520800	19981113 <--
US 2001048921	A1	20011206	US 1998-191970	19981113 <--
US 6558662	B2	20030506		
US 2003157077	A1	20030821	US 2003-374302	20030225 <--

PRIORITY APPLN. INFO.:

US 1997-73230P P 19971114 <--
US 1998-191970 A1 19981113 <--
WO 1998-US24209 W 19981113 <--

AB The inventors have discovered that hematol. disorders, e.g., both neoplastic (hematol. **cancers**) and non-neoplastic conditions, can be treated by the induction of mixed chimerism using myeloreductive, but not myeloablative, conditioning. Methods of the invention reduce **GVHD**, especially **GVHD** associated with mismatched allogeneic or xenogeneic donor tissue, yet provide, for example, significant graft-vs.-leukemia (GVL) effect and the like. The method comprises administration of myeloreductive treatment (such as immunosuppressant regimen), introduction of allogeneic donor hematopoietic stem cell to form chimeric bone marrow in the recipient, and an immunosuppressant regimen after donor stem cell introduction to prevent graft-vs.-host response. The immunosuppressant regimen includes depletion of host T lymphocytes and/or NK cells by treating with anti-CD4 or CD8 antibodies, anti-thymocyte globulin, anti-lymphoblast globulin, thymic irradiation, and cytoreductive agents (e.g. alkylating agents, alkyl sulfonates, nitrosoureas, triazenes, antimetabolites, pyrimidine or purine analogs, vinca alkaloids, epipodophyllotoxins, antibiotics, and others).

```
=> d que stat 116
.L5      5 SEA FILE=REGISTRY ABB=ON (PREDNISONE OR PREDNISOLONE OR
CYCLOSPORINE OR METHOTREXATE OR TACROLIMUS)/CN
L6      1 SEA FILE=REGISTRY ABB=ON BECLOMETHASONE 17,21-DI PROPIONATE/CN
L7      1030 SEA FILE=HCAPLUS ABB=ON (?HEMATOPOIETIC? (3W)?CELL? (3A)?TRANSPL
ANT)
L8      173 SEA FILE=HCAPLUS ABB=ON L7 AND (?GVHD? OR ?GRAFT? (W)V(W)?HOST?
(W)?DISEASE?)
L10     67 SEA FILE=HCAPLUS ABB=ON L8 AND (?CANCER? OR ?CARCIN? OR
?NEOPLASM? OR ?TUMOR? OR ?TUMOUR?)
L11     1 SEA FILE=HCAPLUS ABB=ON L10 AND (L6 OR ?BECLOMETHASONE-17,21-D
I PROPIONAT?)
L12     26 SEA FILE=HCAPLUS ABB=ON L10 AND (L5 OR ?PREDNISONE? OR
?PREDNISOLONE? OR ?CYCLOSPORINE? OR ?METHOTREXAT? OR ?ANTI? (W)?LYMPHOCYTE? (W)?GLOBULIN? OR ?ANTI? (W)T (W)?CELL? (W)(MONOCLONAL? (W)?ANTIBOD? OR ?IMMUNOTOXIN?))
L13     26 SEA FILE=HCAPLUS ABB=ON L11 OR L12
L15     24 SEA L13
L16     16 DUP REMOV L15 (8 DUPLICATES REMOVED)
```

=> d ibib abs 116 1-16

L16 ANSWER 1 OF 16 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED.
on STN

ACCESSION NUMBER: 2005209012 EMBASE
TITLE: Allogeneic hematopoietic cell transplantation for infants
with acute lymphoblastic leukemia.
AUTHOR: Sanders J.E.; Im H.J.; Hoffmeister P.A.; Gooley T.A.;
Woolfrey A.E.; Carpenter P.A.; Andrews R.G.; Bryant E.M.;
Appelbaum F.R.
CORPORATE SOURCE: J.E. Sanders, Fred Hutchinson Cancer Res. Center, Clinical
Research Division, 1100 Fairview Ave N, Seattle, WA 98109,
United States. jsanders@fhcrc.org
SOURCE: Blood, (1 May 2005) Vol. 105, No. 9, pp. 3749-3756.
Refs: 48
ISSN: 0006-4971 CODEN: BLOOAW
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 025 Hematology
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 20050602
Last Updated on STN: 20050602

AB The role of transplantation in infants with acute lymphoblastic leukemia (ALL) is not defined. We analyzed results of 40 infants diagnosed before age 12 months who received a **hematopoietic cell transplant** (HCT) between July 1982 and February 2003 in first complete remission (CR1; n = 17), CR2/3 (n = 7), or relapse (n = 16). Patients were conditioned with cyclophosphamide with total body irradiation (n = 39) or busulfan (n = 1). Donors were matched related (n = 8), mismatched related (n = 16), or un-related (n = 16). Graft-versus-host disease (**GVHD**) prophylaxis was **methotrexate** or **cyclosporine** (n = 7) or **methotrexate** plus **cyclosporine** (n = 33). Thirty-nine patients engrafted, 20 developed acute **GVHD**, and 7 developed chronic **GVHD**. Sixteen patients relapsed and 7 died of other causes. Patients in CR1 had disease-free survival (DFS) of 76% compared with 45% for CR2/CR3 and 8% for relapse (P < .001). Of 33 patients with cytogenetic data, 26 (79%) had MLL gene rearrangement. Fourteen of these

26 were in CR1 and 11 survive in remission. Outcome was associated with phase of disease, but having the MLL gene was not a factor predictive of outcome. Late effects included growth and other hormone deficiencies. These data demonstrate that infants with ALL and MLL gene have excellent DFS when they received transplants in CR1, and consideration for transplantation in CR1 is warranted. .COPYRGT. 2005 by The American Society of Hematology.

L16 ANSWER 2 OF 16 MEDLINE on STN
 ACCESSION NUMBER: 2004635617 MEDLINE
 DOCUMENT NUMBER: PubMed ID: 15610251
 TITLE: Acute renal failure after myeloablative
hematopoietic cell transplant:
 incidence and risk factors.
 AUTHOR: Hingorani Sangeeta R; Guthrie Katherine; Batchelder Ami;
 Schoch Gary; Aboulhosn Nada; Manchion Janel; McDonald
 George B
 CORPORATE SOURCE: Department of Pediatrics and Medicine, University of
 Washington, Seattle, Washington, USA..
 sangeeta.hingorani@seattlechildrens.org
 CONTRACT NUMBER: CA15704 (NCI)
 CA18029 (NCI)
 K23 DK 63038 (NIDDK)
 SOURCE: Kidney international, (2005 Jan) 67 (1) 272-7.
 Journal code: 0323470. ISSN: 0085-2538.
 PUB. COUNTRY: United States
 DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
 LANGUAGE: English
 FILE SEGMENT: Priority Journals
 ENTRY MONTH: 200506
 ENTRY DATE: Entered STN: 20041222
 Last Updated on STN: 20050622
 Entered Medline: 20050621

AB BACKGROUND: Survival after myeloablative therapy followed by **hematopoietic cell transplant** (HCT) is limited by substantial treatment-related toxicities. Acute renal failure (ARF) develops in 25% to 50% of patients after HCT. METHODS: One hundred forty-seven patients were followed prospectively from time of transplant. ARF was defined as a doubling of baseline serum creatinine at any time during the first 100 days post-transplant. We conducted a nested case-control study to identify precipitants of ARF. For each person who developed ARF, 2 controls were selected at random from patients who had not developed ARF as of that time. An exposure period was defined for each case as the 2 weeks prior to the day on which the matched case met the criteria for ARF. The risk of ARF in relation to demographic and anthropometric characteristics, and to types of treatment and comorbidity, was examined using univariable and multivariable conditional logistic regression models. Odds ratios for the associations with ARF were estimated, taking into account the matching. RESULTS: Fifty-three patients (36%) developed ARF at a median of 33 days after transplant (range 1 to 97). Elevated risks were observed in patients who received liposomal amphotericin (OR 6.58; 95%CI 1.45-29.95) and conventional (OR 3.60; 95%CI 0.79-16.55), and in those patients with sinusoidal obstruction syndrome (SOS) (previously termed veno-occlusive disease) (OR 9.37; 95%CI 2.29-38.38). For every 0.1 mg/dL increase in baseline serum Cr, the risk of ARF decreased by 30%. Neither total body irradiation (TBI) dose, levels of metabolites of cyclophosphamide, sepsis, acute graft versus host disease (GVHD), nor **cyclosporine** (CSA) levels was associated with an increased risk of ARF. CONCLUSION: The cumulative

incidence of ARF after HCT remains high. Amphotericin use during the 2-week exposure period and presence of hepatic sinusoidal injury increased the risk of ARF within the first 100 days after HCT. Higher levels of serum creatinine at baseline were associated with a lower risk of ARF.

L16 ANSWER 3 OF 16 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED.
on STN

ACCESSION NUMBER: 2005322961 EMBASE

TITLE: Risk factors for bronchiolitis obliterans in allogeneic hematopoietic stem-cell transplantation for leukemia.

AUTHOR: Santo Tomas L.H.; Loberiza Jr. F.R.; Klein J.P.; Layde P.M.; Lipchik R.J.; Rizzo J.D.; Bredeson C.N.; Horowitz M.M.

CORPORATE SOURCE: Dr. L.H. Santo Tomas, Division of Pulmonary and Critical Care Medicine, Medical College of Wisconsin, 9200 West Wisconsin Ave, Milwaukee, WI 53226, United States.

santo@mcw.edu

SOURCE: Chest, (2005) Vol. 128, No. 1, pp. 153-161.

Refs: 62

ISSN: 0012-3692 CODEN: CHETBF

COUNTRY: United States

DOCUMENT TYPE: Journal; Article

FILE SEGMENT: 015 Chest Diseases, Thoracic Surgery and Tuberculosis

016 Cancer

017 Public Health, Social Medicine and Epidemiology

025 Hematology

037 Drug Literature Index

LANGUAGE: English

SUMMARY LANGUAGE: English

ENTRY DATE: Entered STN: 20050818

Last Updated on STN: 20050818

AB Study objectives: Reported risk factors for bronchiolitis obliterans (BO) in allogeneic **hematopoietic stem-cell transplant** recipients come from modest-sized studies and are limited to experiences of single institutions. We sought to identify risk factors for BO using data from the International Bone Marrow Transplant Registry. Methods: Registry data on 6,275 adult patients with leukemia who received human leukocyte antigen-identical sibling transplants from 1989 to 1997 and survived at least 100 days after transplantation were evaluated for the study. Risk factors for BO were analyzed using proportional hazards regression. Results: Seventy-six patients were found to have BO, with an incidence rate of 1.7% at 2 years after transplantation. The Kaplan-Meier estimate of median time to onset of BO was 431 days. Histologic evaluation was performed in 36 patients (47%). In 28 patients (37%), diagnosis was based on pulmonary function tests, CT scans of the chest, or a combination of both. On multivariate analysis, the factors that were associated with an increased risk for BO included the following: peripheral blood-derived stem cell, a busulfan-based conditioning regimen, interval from diagnosis to transplant \geq 14 months, female donor to male recipient sex match, prior interstitial pneumonitis, and an episode of moderate-to-severe acute graft-vs-host disease (**GVHD**). Conclusion: In addition to corroborating previously reported risk factors, such as acute **GVHD** and a busulfan-based conditioning regimen, we found that peripheral blood stem-cell transplantation, long duration to transplant, female donor to male recipient, and a prior episode of interstitial pneumonitis are associated with an increased risk for BO.

L16 ANSWER 4 OF 16 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED.
 on STN

ACCESSION NUMBER: 2005060091 EMBASE
 TITLE: Outcomes of transplantation with partial T-cell depletion
 of matched or mismatched unrelated or partially matched
 related donor bone marrow in children and adolescents with
 leukemias.

AUTHOR: Bunin N.; Aplenc R.; Leahey A.; Magira E.; Grupp S.;
 Pierson G.; Monos D.

CORPORATE SOURCE: Dr. N. Bunin, Division of Oncology, Children's Hospital of
 Philadelphia, 34th and Civic Center Blvd., Philadelphia, PA
 19104, United States. buninn@email.chop.edu

SOURCE: Bone Marrow Transplantation, (2005) Vol. 35, No. 2, pp.
 151-158.
 Refs: 31
 ISSN: 0268-3369 CODEN: BMTRE
 COUNTRY: United Kingdom
 DOCUMENT TYPE: Journal; Article
 FILE SEGMENT: 007 Pediatrics and Pediatric Surgery
 016 Cancer
 025 Hematology
 026 Immunology, Serology and Transplantation
 037 Drug Literature Index
 038 Adverse Reactions Titles
 LANGUAGE: English
 SUMMARY LANGUAGE: English
 ENTRY DATE: Entered STN: 20050218
 Last Updated on STN: 20050218

AB Graft-versus-host disease (**GVHD**) remains a major barrier to
 successful **hematopoietic stem cell transplant**
 for patients who lack a matched related donor. Partial T-cell depletion
 (TCD) of the graft may decrease the risk of severe **GVHD** with
 unrelated donors (URD) and partially matched related donors (PMRD) while
 retaining an antileukemic effect. We analyzed our experience using URD
 and PMRD for pediatric patients with leukemias from 1990 to 2001. A
 subgroup of 'matched' URD donor pairs was retrospectively analyzed for
 high-resolution class I. Partial TCD was accomplished with monoclonal
 antibody T10B9 or OKT3 and complement. There were 76 URD (45% matched)
 and 28 PMRD recipients. Event-free survival (EFS) was 38.3%, and overall
 survival (OS) 45.1% at 3 years. On multivariate analysis, there was no
 difference in survival based upon marrow source, but nonrelapse mortality
 was higher with the use of PMRD. Relapse occurred in 6% of ALL patients,
 and 22.8% of AML/MDS patients. Grades III-IV **GVHD** was observed
 in only 6.7% of patients. Partial TCD allows use of matched or mismatched
 URD, or PMRD with little mortality from **GVHD**, durable
 engraftment, and no increase in relapse risk. .COPYRGT. 2005 Nature
 Publishing Group All rights reserved.

L16 ANSWER 5 OF 16 MEDLINE on STN DUPLICATE 1
 ACCESSION NUMBER: 2004201882 MEDLINE
 DOCUMENT NUMBER: PubMed ID: 14990986
 TITLE: A novel reduced intensity regimen for allogeneic
 hematopoietic stem cell transplantation associated with a
 reduced incidence of graft-versus-host disease.
 AUTHOR: Miller K B; Roberts T F; Chan G; Schenkein D P; Lawrence D;
 Sprague K; Gorgun G; Relias V; Grodman H; Mahajan A; Foss F
 M
 CORPORATE SOURCE: Department of Medicine, Bone Marrow Transplantation and
 Hematological Malignancy Unit, Beth Israel Deaconess

SOURCE: Medical Center, Boston, MA 02215, USA..
 kbmiller@BIDMC.harvard.edu
 PUB. COUNTRY: Bone marrow transplantation, (2004 May) 33 (9) 881-9.
 DOCUMENT TYPE: Journal code: 8702459. ISSN: 0268-3369.
 LANGUAGE: England: United Kingdom
 FILE SEGMENT: (CLINICAL TRIAL)
 ENTRY MONTH: Journal; Article; (JOURNAL ARTICLE)
 ENTRY DATE: English
 Priority Journals
 200411
 Entered STN: 20040422
 Last Updated on STN: 20041219
 Entered Medline: 20041119

AB Summary: In all, 55 patients at high risk or ineligible for a conventional allogeneic **hematopoietic stem cell transplant** (HSCT) received a regimen consisting of extracorporeal photopheresis, pentostatin, and reduced dose total body irradiation. The median age was 49 years (18-70 years); 44 received a sibling and 11 an unrelated HSCT; 44% were over the age of 50 years and 31% had undergone a prior HSCT. Graft-versus-host disease (**GVHD**) prophylaxis consisted of **cyclosporine** and **methotrexate**. Full donor chimerism was documented in 98% by day +100. The 1000-day nonrelapse mortality was 11%. The median follow-up is 502 days (154-1104 days). The 1- and 2-year overall survival (OS) and event-free survival (EFS) are 67, 58 and 55%, and 47%, respectively. Patients who had not received a prior HSCT or had less than three prior chemotherapy regimens had a 71% OS and 67% EFS at 1 year. Greater than grade II **aGVHD** developed in 9% and chronic **GVHD** (**cGVHD**) in 43%, and extensive in 12% and limited in 31%. Of the patients, 86% who engrafted had a disease response, 72% had complete and 14% partial responses. This novel reduced intensity preparative regimen was well tolerated and associated with a low incidence of transplant-related mortality and serious acute and **cGVHD**.

L16 ANSWER 6 OF 16 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED.
 on STN

ACCESSION NUMBER: 2004517300 EMBASE
 TITLE: Differential diagnosis of cholestasis following allogeneic hematopoietic stem cell transplantation in children: The contribution of serum bile acid levels in relation to other liver function tests.

AUTHOR: Zakrzewski J.L.; Ballauff A.; Wieland R.; Basu O.; Kremens B.

CORPORATE SOURCE: Dr. B. Kremens, University Hospitals of Essen, Dept. of Pediat. Hematol., Oncol./E., Hufelandstr. 55, 45122 Essen, Germany. bernhard.kremens@uni-essen.de

SOURCE: Pediatric Hematology and Oncology, (2004) Vol. 21, No. 8, pp. 697-705.
 Refs: 16
 ISSN: 0888-0018 CODEN: PHONEN

COUNTRY: United States
 DOCUMENT TYPE: Journal; Article
 FILE SEGMENT: 005 General Pathology and Pathological Anatomy
 007 Pediatrics and Pediatric Surgery
 025 Hematology
 037 Drug Literature Index
 048 Gastroenterology

LANGUAGE: English
 SUMMARY LANGUAGE: English
 ENTRY DATE: Entered STN: 20041228

Last Updated on STN: 20041228

. AB Hepatic complications associated with cholestasis occur frequently in hematopoietic stem cell transplant recipients. Since bile acid seems to be a sensitive indicator of beginning cholestasis, the authors monitored total serum bile acid levels in addition to the standard liver function tests in 23 recipients of allogeneic transplants between June 1999 and September 2000. The observations suggest that bile acid is an early and sensitive marker of hepatic **GvHD** but not as specific as bilirubin. For cholestasis in absence of hepatic **GvHD** bile acid seems to be more sensitive than bilirubin. Routinely monitoring of bile acid after hematopoietic stem cell transplantation is not indicated.

L16 ANSWER 7 OF 16 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED.
on STN

ACCESSION NUMBER: 2003413766 EMBASE
 TITLE: Infliximab use in patients with severe graft-versus-host disease and other emerging risk factors of non-Candida invasive fungal infections in allogeneic hematopoietic stem cell transplant recipients: A cohort study.
 AUTHOR: Marty F.M.; Lee S.J.; Fahey M.M.; Alyea E.P.; Soiffer R.J.; Antin J.H.; Baden L.R.
 CORPORATE SOURCE: F.M. Marty, Brigham and Women's Hospital, Division of Infectious Diseases, PBB-A4, 75 Francis St, Boston, MA 02115, United States. fmarty@partners.org
 SOURCE: Blood, (15 Oct 2003) Vol. 102, No. 8, pp. 2768-2776.
 Refs: 45
 ISSN: 0006-4971 CODEN: BLOOAW
 COUNTRY: United States
 DOCUMENT TYPE: Journal; Article
 FILE SEGMENT:
 004 Microbiology
 016 Cancer
 025 Hematology
 026 Immunology, Serology and Transplantation
 037 Drug Literature Index
 LANGUAGE: English
 SUMMARY LANGUAGE: English
 ENTRY DATE: Entered STN: 20031106
 Last Updated on STN: 20031106

AB Acute graft-versus-host disease (**GVHD**) is a common complication of allogeneic hematopoietic stem cell transplantation (HSCT). It has been proposed that **tumor** necrosis factor α (TNF- α) blockade with infliximab may be an effective treatment for severe (grades III-IV) **GVHD**. We determined if infliximab use in this high-risk population was associated with an additional increased risk of non-Candida invasive fungal infections (IFIs). Records of the 2000-2001 HSCT cohort at our institution were reviewed. Fifty-three (20%) of 264 evaluable patients developed severe **GVHD** and 11 of these 53 (21%) received infliximab for treatment. Proven or probable IFI was documented in 10 (19%) of 53 patients with severe **GVHD** (incidence rate of 0.99 cases/1000 **GVHD** patient-days). When stratified by infliximab use, 5 of 11 infliximab recipients developed an IFI (6.78 cases/1000 **GVHD** patient-days), compared with 5 of 42 IFI cases among nonrecipients (0.53 cases/1000 **GVHD** patient-days). In a time-dependent Cox regression model among patients with severe **GVHD**, the adjusted IFI hazard ratio of infliximab exposure was 13.6 ($P = .004$; 95% CI, 2.29-80.2). We conclude that infliximab administration is associated with a significantly increased risk of

non-Candida IFI in HSCT recipients with severe **GVHD** disease.
 Pre-emptive systemic antifungal therapy against molds should be considered in patients who develop severe **GVHD** after HSCT if infliximab is used. .COPYRGT. 2003 by The American Society of Hematology.

L16 ANSWER 8 OF 16 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN
 ACCESSION NUMBER: 2004:152543 BIOSIS
 DOCUMENT NUMBER: PREV200400147930
 TITLE: Reduced intensity conditioning regimen (RIC) with CD 45 monoclonal antibodies for stem cell transplantation using matched unrelated (MUD) or mismatched donors.
 AUTHOR(S): Popat, Uday [Reprint Author]; Carrum, George [Reprint Author]; Kuehnle, Ingrid [Reprint Author]; Bollard, Catherine; Gottschalk, Stephen; Heslop, Helen [Reprint Author]; Krance, Robert; Brenner, Malcolm [Reprint Author]
 CORPORATE SOURCE: Department of Medicine, Baylor College of Medicine, Houston, TX, USA
 SOURCE: Blood, (November 16 2003) Vol. 102, No. 11, pp. 705a.
 print.
 Meeting Info.: 45th Annual Meeting of the American Society of Hematology. San Diego, CA, USA. December 06-09, 2003.
 American Society of Hematology.
 CODEN: BLOOAW. ISSN: 0006-4971.
 DOCUMENT TYPE: Conference; (Meeting)
 Conference; (Meeting Poster)
 Conference; Abstract; (Meeting Abstract)
 LANGUAGE: English
 ENTRY DATE: Entered STN: 17 Mar 2004
 Last Updated on STN: 17 Mar 2004

AB **Hematopoietic stem cell transplant** using RIC decreases morbidity and mortality thereby allowing it to be offered to patients who are otherwise not candidates for allogeneic blood stem cell transplants, because of age or co-morbidity. For optimal **antitumor** effect, complete donor chimerism is likely necessary. Unfortunately, many current conditioning regimens result in mixed chimerism or in graft rejection, and may require post transplant manipulations, such as reduction of immunosuppression that increase the risks of severe **GvHD**. Based on a successful murine model, we have investigated whether CD45 monoclonal antibody (MAb) can deplete recipient immune and hematopoietic cells and facilitate donor engraftment in subablative transplantation of matched unrelated or mismatched unrelated or family donor stem cells. We used two rat anti CD45 monoclonal antibodies against non overlapping epitopes on the CD 45 molecules at a dose of 400 mcg/kg/dayX4 added to our standard RIC regimen of TBI 450 cGY, Fludarabine 120mg/m², and Campath 1H (30 mg), and FK506 as **GvHD** prophylaxis. 12 patients with hematological malignancies, not eligible for standard transplant because of age or co-morbidities have been enrolled to date. Reasons for reduced intensity transplant included age >55(6 pts), second transplant (5 pts.), Previous fungal infection (2pts.); and abnormal liver (3 pts), kidney (3 pts), cardiac (2 pts) or pulmonary function (3 pts). Median age is 42 yrs (range 1-65 yrs). 7 patients were male, 5 female. 5 patients had MDS or AML, 3 ALL, 2 HD, 1CLL/AA, and 1 NHL. 6 patients were in relapse with active disease and 6 were in complete remission (4 CR1, 2 CR2) at the time of transplant. 9 patients or donors were CMV positive. 5 donors were HLA identical (6/6) but unrelated and 7 donors had one antigen mismatch. (5 unrelated, 2 family). All but one patient received peripheral blood stem cells. All 12 patients engrafted. Median time to neutrophil engraftment was 12 days (8-18). By day 30 all the patients were 100% donor chimera, including all

7 patients who had one antigen mismatched (5/6) donors and the 3 patients who had rejected a previous transplant. 1 patient had grade III-IV severe **GvHD**, and 1 had grade II **GvHD**. 1 patient died of progressive disease. 11 patients are alive (10 disease free) 29-279 days (median 116 days) post transplant. We compared the engraftment data with 16 patients (10 MUD, 6 Mismatched donor-5/6) treated on our previous protocol using the same conditioning regimen without CD 45 MAb. 4 of 16 patients rejected their graft compared to none of the patients in current study. Of the 6 donors in this earlier series who received mismatched grafts, 3 rejected, compared to 0/7 following the addition of CD45 MAbs ($p=0.07$, two tailed Fisher exact test). We are continuing further accrual on this study to determine if this trend to improved engraftment continues. These data suggest that the addition of CD45 MAb to subablate conditioning regimens is safe, may contribute to establishment of complete donor chimerism, and may be of particular value when transplantation uses HLA mismatched donor stem cells.

L16 ANSWER 9 OF 16 MEDLINE on STN DUPLICATE 2
 ACCESSION NUMBER: 2003490760 MEDLINE
 DOCUMENT NUMBER: PubMed ID: 14569561
 TITLE: Reduced-intensity allogeneic stem cell transplantation for patients whose prior autologous stem cell transplantation for hematologic malignancy failed.
 AUTHOR: Fung H C; Cohen S; Rodriguez R; Smith D; Krishnan A; Somlo G; Sahebi F; Senitzer D; O'Donnell M R; Stein A; Snyder D S; Spielberger R; Bhatia R; Falk P; Molina A; Nademanee A; Parker P; Kogut N; Popplewell L; Vora N; Margolin K; Forman S J
 CORPORATE SOURCE: Division of Hematology and Bone Marrow Transplantation, Kaiser Permanente-City of Hope BMT Program, City of Hope Cancer Center, 1500 E. Duarte Road, Duarte, CA 91010, USA.. hfung@coh.org
 CONTRACT NUMBER: CA 33572 (NCI)
 P01 CA 30206 (NCI)
 SOURCE: Biology of blood and marrow transplantation : journal of the American Society for Blood and Marrow Transplantation, (2003 Oct) 9 (10) 649-56.
 Journal code: 9600628. ISSN: 1083-8791.
 PUB. COUNTRY: United States
 DOCUMENT TYPE: (CLINICAL TRIAL)
 LANGUAGE: English
 FILE SEGMENT: Priority Journals
 ENTRY MONTH: 200406
 ENTRY DATE: Entered STN: 20031022
 Last Updated on STN: 20040625
 Entered Medline: 20040624
 AB Autologous hematopoietic stem cell transplantation (autoSCT) is an effective treatment for patients with various hematologic malignancies. Despite the significant improvement in the overall outcome, disease progression after transplantation remains the major cause of treatment failure. With longer follow-up, therapy-related myelodysplasia/acute myelogenous leukemia is becoming an important cause of treatment failure. The prognosis for these 2 groups of patients is very poor. Allogeneic hematopoietic stem cell transplantation (alloSCT) is a potential curative treatment for these patients. However, the outcome with conventional myeloablative alloSCT after failed autoSCT is typically poor because of high transplant-related mortality. In an attempt to reduce the treatment-related toxicity, we studied a reduced-intensity conditioning

regimen followed by alloSCT for patients with progressive disease or therapy-related myelodysplasia/acute myelogenous leukemia after autoSCT. This report describes the outcomes of 28 patients with hematologic malignancies who received a reduced-intensity alloSCT after having treatment failure with a conventional autoSCT. Fourteen patients received a **hematopoietic stem cell transplant** from a related donor and 14 from an unrelated donor. The conditioning regimen consisted of low-dose (2 Gy) total body irradiation with or without fludarabine in 4 patients and the combination of melphalan (140 mg/m²) and fludarabine in 24. **Cyclosporine** and mycophenolate mofetil were used for posttransplantation immunosuppressive therapy, as well as graft-versus-host disease (**GVHD**) prophylaxis, in all patients. All patients engrafted and had >90% donor chimerism on day 100 after SCT. Currently, 13 patients (46%) are alive and disease free, 7 patients (25%) developed disease progression after alloSCT, and 8 (32%) died of nonrelapse causes. Day 100 mortality and nonrelapse mortality were 25% and 21%, respectively. With a median follow-up of 24 months for surviving patients, the 2-year probabilities of overall survival, event-free survival, and relapse rates were 56.5%, 41%, and 41.9%, respectively. Six patients (21%) developed grade III to IV acute **GVHD**. Among 21 evaluable patients, 15 (67%) developed chronic **GVHD**. We conclude that (1) reduced-intensity alloSCT is feasible and has an acceptable toxicity profile in patients who have previously received autoSCT and that (2) although follow-up was short, a durable remission may be achieved in some patients who would otherwise be expected to have a poor outcome.

L16 ANSWER 10 OF 16 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN

ACCESSION NUMBER: 2004:181399 BIOSIS
DOCUMENT NUMBER: PREV200400181250
TITLE: Risk factors for severe graft-versus-host disease after nonmyeloablative hematopoietic cell transplantation for treatment of hematological malignancies.
AUTHOR(S): Flowers, Mary E. D. [Reprint Author]; Traina, Fabiola [Reprint Author]; Storer, Barry [Reprint Author]; Maris, Michael [Reprint Author]; Bethge, Wolfgang [Reprint Author]; Carpenter, Paul [Reprint Author]; Maloney, David [Reprint Author]; Storb, Rainer [Reprint Author]; Sandmaier, Brenda M. [Reprint Author]; Martin, Paul J. [Reprint Author]
CORPORATE SOURCE: Clinical Research Division, Department of Medicine, Fred Hutchinson Cancer Research Center, University of Washington, Seattle, WA, USA
SOURCE: Blood, (November 16 2003) Vol. 102, No. 11, pp. 152a. print.
Meeting Info.: 45th Annual Meeting of the American Society of Hematology. San Diego, CA, USA. December 06-09, 2003.
American Society of Hematology.
CODEN: BLOOAW. ISSN: 0006-4971.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 7 Apr 2004
Last Updated on STN: 7 Apr 2004
AB The efficacy of nonmyeloablative allogeneic **hematopoietic cell transplant** (HCT) depends on the balance between beneficial antineoplastic effects weighed against detrimental effects related to graft-versus-host disease (**GVHD**). Risk factors for

severe, life-threatening **GVHD** were analyzed retrospectively among 171 consecutive patients who had related or unrelated nonmyeloablative HCT for treatment of hematologic malignancies. The conditioning regimen was 2.0 Gy total body irradiation with or without fludarabine, and mycophenolate mofetil and **cyclosporine** were used for post-transplant immunosuppression. Overall, 44 of 171 (26%) patients developed severe **GVHD** with a median follow-up of 30 (range, 12-65) months. The incidence of severe **GVHD** was similar after related and unrelated HCT. Manipulation of immunosuppression to induce graft-versus-leukemia/**tumor** effects in patients with relapsing/persistent disease was not associated with subsequent development of severe **GVHD** ($P=0.98$). In a Cox regression analysis, factors that were significantly associated with severe, life-threatening **GVHD** were: diagnosis of myeloid malignancies ($P=.01$), donor lymphocyte infusion for persistent, progressive or recurrent malignancy ($P=.05$) and, preceding non-severe acute **GVHD** ($P=.002$). The cumulative incidence of severe **GVHD** at 2 years after HCT was 37% among patients with myeloid malignancies, compared to 21% among those with non-myeloid malignancies. Nonrelapse mortality at 3 years after transplant was 33% for patients with myeloid malignancies and 24% for those with non-myeloid malignancies ($P=0.20$). We speculate that the increased risk of severe **GVHD** among patients with myeloid diseases could be related to the antigen-presenting function of malignant myeloid cells. The differences in risk of severe, life-threatening **GVHD** according to myeloid or non-myeloid disease category should be taken into account in the design of future clinical trials.

L16 ANSWER 11 OF 16 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN

ACCESSION NUMBER: 2003:337177 BIOSIS
 DOCUMENT NUMBER: PREV200300337177
 TITLE: Infectious Complications in Long-Term Survivors of Cord Blood Stem Cell Transplantation (CBSCT); Experience at Roswell Park Cancer Institute.
 AUTHOR(S): Alam, Arif R. [Reprint Author]; Varma, Geetha; Hahn, Theresa; Segal, Brahm; Paplham, Pamela; Becker, Joanne; Baer, Maria; Bambach, Barbara; Silva, Joaquin; Slack, James; Wetzler, Meir; McCarthy, Philip L. Jr.
 CORPORATE SOURCE: Medicine, Roswell Park Cancer Institute, Buffalo, NY, USA
 SOURCE: Blood, (November 16 2002) Vol. 100, No. 11, pp. Abstract No. 2479. print.
 Meeting Info.: 44th Annual Meeting of the American Society of Hematology. Philadelphia, PA, USA. December 06-10, 2002.
 American Society of Hematology.
 CODEN: BLOOAW. ISSN: 0006-4971.
 DOCUMENT TYPE: Conference; (Meeting)
 Conference; Abstract; (Meeting Abstract)
 LANGUAGE: English
 ENTRY DATE: Entered STN: 23 Jul 2003
 Last Updated on STN: 23 Jul 2003
 AB Umbilical cord blood is a source of stem cells for patients undergoing unrelated **hematopoietic stem cell transplant**. The recipients are at an increased risk of infectious complications because of slower engraftment kinetics in the acute period post-CBSCT; however, there is no long term data regarding infectious complications post day 100. We investigated the infectious complications in our long-term survivors (LTS) after CBSCT. Between 5/97 and 10/2001, 26 patients received a CBSCT for a hematologic malignancy. 11 patients died before day 100 of infection (n=4), regimen-related toxicity (n=4),

GVHD (n=1), recurrent disease (n=1) and graft failure (n=1) and were excluded from this analysis. In the 15 long-term survivors, median age at CBSCT was 34 years (range 5-53 years). Donor-recipient HLA match was 6/6 (n=1), 5/6 (n=6), or 4/6 (n=8). Seven patients had sex mismatched CB donors. **AGVHD** prophylaxis was **Cyclosporine** (CsA), **Methylprednisolone** (MP) regimen (n=12), or CsA, MP and ATG (n=3). CsA was changed to FK506 in 7 patients due to CsA toxicity. Median nucleated cell dose was 2.25 (range, 0.134-0.423) x 10⁷/kg and median CD34+ cell dose was 0.115 (range, 0.025-0.191) x 10⁶/kg). Median time to ANC>500/mm³ was 34 days (range, 16-104) and median time to platelet count >20,000/mm³ was 66 days (range, 41-144). Median follow-up post CBSCT in the long-term survivors was 33.7 months (range 5.4 - 47.1). 5 of the 15 LTS developed chronic graft-versus-host disease (**cGVHD**) (limited n=1, extensive n=4). 6 of the 15 LTS developed opportunistic infections (herpes zoster n=1, disseminated invasive aspergillosis n=2, localized pulmonary aspergillosis n=1, disseminated candida glabrata n=1, pulmonary atypical mycobacterium infection n=1). 3 of the 6 patients with opportunistic infections have died of refractory leukemia (n=1), relapsed leukemia (n=1) or multi-organ failure due to infection (n=1). The remaining patients were either successfully treated (resection of localized pulmonary aspergillosis n=1) or are currently receiving active treatment for fungal disease n=2, and atypical mycobacterium n=1. At the time of this report, 4 of the 15 LTS have died. Patients post CBSCT remain at risk for opportunistic infections. This risk appears to be increased in patients who develop **cGVHD** and require immunosuppression. Selected patients may benefit from more aggressive anti-microbial prophylaxis to prevent opportunistic infections during immunosuppressive therapy.

L16 ANSWER 12 OF 16 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN

ACCESSION NUMBER: 2003:336363 BIOSIS
 DOCUMENT NUMBER: PREV200300336363

TITLE: Kinetics of Mixed Chimerism in Peripheral Blood Hematopoietic Subpopulations from 120 Patients after Nonmyeloablative **Hematopoietic Stem Cell Transplant**.

AUTHOR(S): Little, Marie-Terese [Reprint Author]; Baker, Jennifer E. [Reprint Author]; Sandmaier, Brenda M. [Reprint Author]; Maris, Michael B. [Reprint Author]; Maloney, David [Reprint Author]; Gooley, Theodore [Reprint Author]; Oparin, Dmitrij [Reprint Author]; Zellmer, Eustacia [Reprint Author]; Mielcarek, Marco [Reprint Author]; Wagner, John [Reprint Author]; Shizuru, Judith [Reprint Author]; Blume, Karl [Reprint Author]; Chauncey, Thomas [Reprint Author]; Storb, Rainer [Reprint Author]

CORPORATE SOURCE: Clinical Research Division, Fred Hutchinson Cancer Research CTR, Seattle, WA, USA

SOURCE: Blood, (November 16 2002) Vol. 100, No. 11, pp. Abstract No. 136. print.
 Meeting Info.: 44th Annual Meeting of the American Society of Hematology. Philadelphia, PA, USA. December 06-10, 2002. American Society of Hematology.

CODEN: BLOOAW. ISSN: 0006-4971.

DOCUMENT TYPE: Conference; (Meeting)
 Conference; (Meeting Poster)
 Conference; Abstract; (Meeting Abstract)

LANGUAGE: English

ENTRY DATE: Entered STN: 23 Jul 2003

Last Updated on STN: 23 Jul 2003

AB The kinetics of donor engraftment in peripheral blood hematopoietic subpopulations from 120 patients (median age 54 years) undergoing nonmyeloablative hematopoietic stem cell transplantation (HSCT) were analyzed. The nonmyeloablative approach consisted of total body irradiation (200 cGy), marrow (n=10) or PBSC (n=110) allografts, and postgrafting immunosuppression with mycophenolate mofetil and cyclosporine. Sixty-two percent of the patients received fludarabine (30mg/m² on days -4, -3, -2) before HSCT. Patients received either HLA matched related (n=87) or unrelated donor (n=33) HSCT for cervical cancer (n=1) or hematologic malignancies (n=119) including ALL (n=2), AML (n=17), CLL (n=13), CML (n=14), HD (n=11), MDS (n=19), MM (n=24), NHL (n=19). Graft rejection or failure occurred in 12/120 (10%) of patients. Acute GVHD of grades II and III-IV occurred in 41% and 13% of patients, respectively. Peripheral blood samples were sorted on post-transplant days 14, 28, 42, 56, 84, 180 and 365 by multidimensional FACS into CD3+CD56- (T-lymphocytes), CD3+CD4+CD8- (CD4+ T-lymphocytes), CD3+CD4-CD8+ (CD8+ T-lymphocytes) CD45+side scatter mid-hi (granulocytes), CD56+CD3- (NK cells), and CD14+CD3- CD56- (monocytes) fractions. Percentages of donor chimerism were analyzed by PCR-based VNTR analyses and quantified by phosphoimage analyses. On day 14 post-transplant, the highest degree of donor reconstitution was noted in the NK fraction followed by CD8+ T-lymphocytes, CD3+ lymphocytes, CD4+ T-lymphocytes, monocytes, and granulocytes. On day 28, donor granulocyte chimerism rapidly increased, followed by progressive increases in the remaining cell populations. Most patients remained mixed donor/host chimeras for extended periods of time (at least to 180 days post-transplant) with greater than 60% donor chimerism in each subpopulation. This pattern of donor reconstitution was consistent for all of the patients with hematologic malignancies except those with CML and MDS where percentages of donor T-lymphocyte chimerisms were lower. Patients receiving PBSC product had a higher degree of donor T lymphocyte chimerism than recipients of marrow ($p=.02$). Greater intensity of therapy before HSCT was associated with higher degrees of donor granulocyte, CD3+ lymphocyte, and monocyte chimerisms. The association of donor chimerism with survival and progression-free survival was assessed by Cox regression analysis, and donor chimerism was treated as a time-dependent covariate. A high degree of donor NK cell chimerism was consistently associated with improved overall survival and progression-free survival ($p=.02$ and .002, respectively). The CD4/CD8 absolute cell ratio was consistently >1 immediately after transplant in the 38 patients that were analyzed. There was no correlation with CD4 donor chimerism nor absolute cell counts and overall survival. There was a suggestion that increased donor CD8 chimerism was associated with decreased risk of mortality before ($p=.05$) and after ($p=.08$) adjusting for absolute donor counts in this smaller sample size (n=38). These results suggest that monitoring mixed chimerism early after transplant is important for determining outcomes and for the development of new strategies for intervention.

L16 ANSWER 13 OF 16 MEDLINE on STN

DUPLICATE 3

ACCESSION NUMBER: 2002016110 MEDLINE

DOCUMENT NUMBER: PubMed ID: 11418375

TITLE: Conventional hematopoietic stem cell transplants from identical or alternative donors are feasible in recipients relapsing after an autograft.

AUTHOR: di Grazia C; Raiola A M; Van Lint M T; Lamparelli T; Gualandi F; Berisso G; Bregante S; Dominietto A; Mordini N; Bruno B; Frassoni F; Bacigalupo A

CORPORATE SOURCE: Dipartimento di Ematologia, Ospedale San Martino, Genoa,

SOURCE: Italy.. emato2@smartino.ge.it
 Haematologica, (2001 Jun) 86 (6) 646-51.
 Journal code: 0417435. ISSN: 0390-6078.

PUB. COUNTRY: Italy
 DOCUMENT TYPE: (EVALUATION STUDIES)
 Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English
 FILE SEGMENT: Priority Journals
 ENTRY MONTH: 200201
 ENTRY DATE: Entered STN: 20020121
 Last Updated on STN: 20020124
 Entered Medline: 20020102

AB BACKGROUND AND OBJECTIVES: The risk of relapse after autologous bone marrow transplantation (ASCT) is high and is related to the type of malignancy and phase of the disease. The outcome for the patient who relapses after an autologous transplant is poor. Some of these patients achieve a remission with conventional chemotherapy, but it is usually short-lasting. Most of them succumb to the original disease. One further therapeutic possibility is an allogeneic transplant which would confer the potential advantage of a graft-versus-leukemia effect in addition to the lack of tumor contamination of the graft and to a high-dose intensity conditioning regimen. DESIGN AND METHODS: We have studied the outcome of 31 patients with hematologic malignancies who underwent an allogeneic hematopoietic stem cell transplant (HSCT) after failing an autologous transplant because of relapse (n=29) or persistent aplasia (n=2). The median age at allograft was 36 years (18-55) and the interval from autograft to allograft was 21 months (3-141). The source of stem-cells was unmanipulated bone marrow (n=26) or growth-factor-mobilized peripheral blood (n=5). The donor was an HLA-identical sibling (n=7), or an alternative donor (n=24) (family mismatched n=11, or matched unrelated n=13). The conditioning regimen was cyclophosphamide and thiotapec (n=22), or cyclophosphamide and total body irradiation (n=9) Graft-versus-host disease (GvHD) prophylaxis consisted of cyclosporine (CyA) + methotrexate (MTX).
 RESULTS: Acute GvHD was scored as 0-I, II, or III-IV in 39%, 48%, and 13% of the patients, respectively. Sixteen patients died of transplant-related complications and one of progressive disease. With a median follow-up of 220 days (9-2104) the actuarial 2-year transplant-related mortality (TRM) was 51%, the actuarial relapse risk 37%, the actuarial survival 46%. Fifteen patients (48%) are alive in complete remission, with a median follow-up of 32 months (range 2-71).
 INTERPRETATION AND CONCLUSIONS: These data suggest that patients relapsing after an autotransplant should be screened for potential related or unrelated donors: although TRM remains high there is a definite chance of long-term disease-free survival if these patients are allografted.

L16 ANSWER 14 OF 16 MEDLINE on STN DUPLICATE 4
 ACCESSION NUMBER: 2001559681 MEDLINE
 DOCUMENT NUMBER: PubMed ID: 11607768
 TITLE: Fludarabine and melphalan-based conditioning for patients with advanced hematological malignancies relapsing after a previous hematopoietic stem cell transplant.
 AUTHOR: Devine S M; Sanborn R; Jessop E; Stock W; Huml M; Peace D; Wickrema A; Yassine M; Amin K; Thomason D; Chen Y H; Devine H; Maningo M; van Besien K
 CORPORATE SOURCE: Stem Cell Transplant Program, University of Illinois College of Medicine, Chicago, IL 60612, USA.
 SOURCE: Bone marrow transplantation, (2001 Sep) 28 (6) 557-62.

JOURNAL CODE: 8702459. ISSN: 0268-3369.
 ·PUB. COUNTRY: England: United Kingdom
 DOCUMENT TYPE: (CLINICAL TRIAL)
 LANGUAGE: Journal; Article; (JOURNAL ARTICLE)
 English
 FILE SEGMENT: Priority Journals
 ENTRY MONTH: 200208
 ENTRY DATE: Entered STN: 20011022
 Last Updated on STN: 20020802
 Entered Medline: 20020801

AB Severe regimen-related toxicity often complicates second transplant procedures performed in patients with hematological malignancies that have relapsed after an initial **hematopoietic stem cell** (HSC) **transplant**. Therefore, we studied the safety and efficacy of a reduced-intensity fludarabine and melphalan based conditioning regimen in 11 patients who had relapsed following an autologous (n = 7) or allogeneic (n = 4) HSC transplant. All patients received allogeneic peripheral blood HSC from either an HLA-identical (n = 7) or an HLA-mismatched (n = 4) relative. Diagnoses included AML (n = 9), ALL (n = 1), or Hodgkin's disease (n = 1). Only one patient was in complete remission at the time of second transplant. The median interval between first transplant and relapse was 163 days (range 58-1885). Recipients of HLA-mismatched transplants received antithymocyte globulin in addition to fludarabine and melphalan as part of the conditioning regimen. All 11 patients received acute **GVHD** prophylaxis consisting of tacrolimus and **methotrexate**. Ten of 11 patients achieved hematopoietic engraftment with a median time to absolute neutrophil count $>0.5 \times 10(9)/l$ and to platelet count of $>20 \times 10(9)/l$ of 14 and 19 days, respectively. All engrafting patients achieved 100% donor chimerism on initial analysis, except for one with persistent leukemia at day +19. Two patients experienced grade 3 regimen-related toxicity, manifesting as acute renal failure. Acute **GVHD** grades 2-4 occurred in two recipients and chronic **GVHD** in four. The 100-day mortality from all causes was 36%. Ten of 11 patients (91%) died a median of 140 days (range 9-996) after the second transplant. The causes of death included relapse (n = 5), sepsis (n = 4), and idiopathic pneumonia syndrome (n = 1). One patient with AML survives in remission at 880 days post-transplant. We conclude that fludarabine- and melphalan-based conditioning promotes full donor chimerism, even following HLA-mismatched transplants. However, the regimen may be more beneficial when applied to patients undergoing allogeneic HSC transplantation earlier in their disease course.

L16 ANSWER 15 OF 16 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN

ACCESSION NUMBER: 2002:241260 BIOSIS
 DOCUMENT NUMBER: PREV200200241260
 TITLE: Analysis of mixed chimerism in peripheral blood hematopoietic subpopulations from 101 patients after nonmyeloablative **hematopoietic stem cell transplant**.

AUTHOR(S): Little, Marie-Terese [Reprint author]; Baker, Jennifer [Reprint author]; Sandmaier, Brenda [Reprint author]; Maris, Michael [Reprint author]; Maloney, David [Reprint author]; Gooley, Theodore [Reprint author]; Zellmer, Eustacia [Reprint author]; Heimfeld, Shelly [Reprint author]; Georges, George [Reprint author]; Wagner, John [Reprint author]; Shizuru, Judith; Blume, Karl; Chauncey, Thomas [Reprint author]; Storb, Rainer [Reprint author]

CORPORATE SOURCE: Fred Hutchinson Cancer Research Center, Seattle, WA, USA
· SOURCE: Blood, (November 16, 2001) Vol. 98, No. 11 Part 1, pp.
477a. print.
Meeting Info.: 43rd Annual Meeting of the American Society
of Hematology, Part 1. Orlando, Florida, USA. December
07-11, 2001. American Society of Hematology.
CODEN: BLOOAW. ISSN: 0006-4971.

DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)

LANGUAGE: English

ENTRY DATE: Entered STN: 17 Apr 2002
Last Updated on STN: 17 Apr 2002

AB Nonmyeloablative hematopoietic stem cell transplantation (HSCT) promotes initial mixed chimerism with limited toxicity. Although the induction of chimerism after allogeneic HSCT has been documented, the kinetics of donor engraftment in different hematopoietic subpopulations as they relate to outcomes have not been extensively studied. Analysis of mixed chimerism was performed in a cohort of 101 patients (median age 54 years) who received either matched related (n=74) or unrelated donor (n=27) nonmyeloablative allogeneic HSCT for a solid **tumor** (n=1) and hematologic malignancies (n=100) including ALL (n=1), AML (n=10), CLL (n=11), CML (n=11), HD (n=11), MDS (n=18), MM (n=24), NHL (n=14). The nonmyeloablative HSCT approach consisted of total body irradiation (200 cGy), bone marrow (n=8) or PBSC (n=93) grafts, and postgrafting immunosuppression with mycophenolate mofetil and **cyclosporine**. In addition, 62% of the patients received fludarabine (30 mg/m² on days -4, -3, -2). Graft rejection or failure occurred in 10% of patients. Acute **GVHD** of grades II-IV and III-IV occurred in 52% and 15% of patients, respectively (56% and 15% for nonrejectors). Peripheral blood samples were sorted on post-transplant days 14, 28, 42, 56, 84, 180 and 365 by multidimensional FACS into CD3+CD56- (T-lymphocytes), CD45+side scattermid-hi (granulocytes), CD56+CD3- (NK cells), and CD14+CD3-CD56- (monocytes) fractions. Percent donor chimerism was analyzed by PCR-based VNTR analysis and quantified by phosphoimage analysis. Cox regression was used to assess the association of donor chimerism with time-to-event outcomes, survival and relapse-free survival. Donor chimerism was treated as a time-dependent covariate in these models. The hazard of mortality was significantly decreased as percent donor granulocyte chimerism increased. If chimerism was modeled as a continuous variable, an increase of 20% chimerism was associated with a decrease in the hazard of mortality of .77 (hazard ratio (HR)=0.77; 95% CI, 0.60 to 0.98; p=.03). Similarly, as the percent donor NK cell and monocyte chimerism increased, the hazard of mortality decreased (HR=0.75; 95% CI, 0.58 to 0.98; p=.03 and HR=0.70; 95% CI, 0.53 to 0.89 p=.004, respectively). Increasing percent donor T-lymphocyte chimerism was associated with a decrease in hazard of mortality but this association was not statistically significant (p=0.38). There were statistically significant associations between high percentages of donor granulocyte, NK and monocyte chimerisms and increased relapse-free survival (p=.005, .0009 and .03, respectively) and a trend towards an association for increased percent donor T-lymphocyte chimerism (p=.14). Logistic regression was used to assess the association of donor chimerism with the probability of grades II-IV **GVHD**, where the last chimerism value before day 28 and before occurrence of **GVHD** was used as a covariate. There was no statistically significant association between the probability of grades II-IV acute **GVHD** and donor chimerism in any of the sorted subpopulations. The evaluation of early donor chimerism maybe a valuable tool for assessing the risk of mortality and relapse-free survival.

L16 ANSWER 16 OF 16 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED.
 on STN

ACCESSION NUMBER: 2001198963 EMBASE
 TITLE: Unrelated cord blood transplant experience by the pediatric
 blood and marrow transplant consortium.
 AUTHOR: Yu L.C.; Wall D.A.; Sandler E.; Chan K.W.; Grayson G.;
 Kletzel M.
 CORPORATE SOURCE: Dr. L.C. Yu, Children's Hospital, 200 Henry Clay Avenue,
 New Orleans, LA 70118, United States. lyu@lsuhsc.edu
 SOURCE: Pediatric Hematology and Oncology, (2001) Vol. 18, No. 4,
 pp. 235-245.
 Refs: 25
 ISSN: 0888-0018 CODEN: PHONEN
 COUNTRY: United States
 DOCUMENT TYPE: Journal; Article
 FILE SEGMENT: 007 Pediatrics and Pediatric Surgery
 025 Hematology
 037 Drug Literature Index
 LANGUAGE: English
 SUMMARY LANGUAGE: English
 ENTRY DATE: Entered STN: 20010628
 Last Updated on STN: 20010628

AB Cord blood (CB) has emerged as a potential source of hematopoietic stem cells for patients who are in need of **hematopoietic stem cell transplant** (HSCT). The authors analyzed the Pediatric Blood and Marrow Transplant Consortium's (PBMTC) data of consecutive unrelated CB transplants performed during the initial 2 years of using placental blood grafts. From January 1995 to December 1996 PBMTC performed a total of 44 unrelated CB transplant for a variety of diseases consisting of acute leukemias ($n = 29$), congenital conditions ($n = 9$), and bone marrow failure ($n = 6$). There were 15 females and 29 males with median age of 5 years (range 0.4-20.6 years) and median weight of 18.2 kg (range 6.3-70 kg). The median volume of CB units was 80 mL (range 44.5-215 mL) and the median cell dose given was 4.3×10^7 /kg of recipient weight (range $1.1-23 \times 10^7$ /kg). Techniques used for human leukocyte antigen (HLA) matching were serologic typing for class I HLA antigens and high-resolution molecular typing for HLA-DRB(1) alleles. HLA disparities were as follows: 4 were 6/6 matches, 21 were 5/6, 15 were 4/6, and 4 were 3/6. Twenty-nine (66 %) of CB units were DRB(1) matched with recipients. Conditioning regimens consisted of either total body irradiation containing ($n = 31$) or chemotherapy only ($n = 11$) regimens. All but 3 patients receive **cyclosporine** as part of graft vs. host disease (**GvHD**) prophylaxis in combination with either **methotrexate** (MTX) or **methylprednisolone** (Pred). The other 3 patients had FK506 and MTX for **GvHD** prophylaxis. Myeloid engraftment (absolute neutrophil count ≥ 500) occurred at a median of 21 days (range 10-43 days) and platelet $\geq 50,000/\text{mm}^3$ was noted at a median of 44 days (range 16-102 days). Eight patients died too early (<day +28) for evaluation of engraftment (5 for infection, 2 for multiorgan failure, 1 for toxic epidermolysis). The probability of having grade II-IV acute **GvHD** for all patients was $44 \pm 0.7\%$. The incidence of a **GvHD** is similar for 4/6 and 5/6 antigen when DRB(1) matched, at 47 and 52%, respectively. Chronic **GvHD** was noted in 28% of patients surviving > 90 days. The Kaplan-Meir estimate of 4-year event-free survival was 43%. A Cox model for analysis of factors associated with survival was DRB(1) matching, $p = .001$; cell dose, $p = .009$; and younger age, $p = .03$. In conclusion, CB transplant offers a good alternative to bone marrow transplant. Although **GvHD** occurs, it is usually of low severity despite the high frequency of multiple HLA

Qazi 09/913,435

14/09/2005

antigen mismatches. It also appears that a 4/6 is as good as a 5/6 matched antigen CB unit when DRB(1) matched especially in the pediatric setting.

```
=> d que stat 117
.L5      5 SEA FILE=REGISTRY ABB=ON (PREDNISONE OR PREDNISOLONE OR
CYCLOSPORINE OR METHOTREXATE OR TACROLIMUS)/CN
.L6      1 SEA FILE=REGISTRY ABB=ON BECLOMETHASONE 17,21-DIPROPIONATE/CN
.L7      1030 SEA FILE=HCAPLUS ABB=ON (?HEMATOPOIETIC? (3W) ?CELL? (3A) ?TRANSPL
ANT)
.L8      173 SEA FILE=HCAPLUS ABB=ON L7 AND (?GVHD? OR ?GRAFT? (W) V(W) ?HOST?
(W) ?DISEASE?)
.L10     67 SEA FILE=HCAPLUS ABB=ON L8 AND (?CANCER? OR ?CARCIN? OR
?NEOPLASM? OR ?TUMOR? OR ?TUMOUR?)
.L11     1 SEA FILE=HCAPLUS ABB=ON L10 AND (L6 OR ?BECLOMETHASONE-17,21-D
I PROPIONAT?)
.L12     26 SEA FILE=HCAPLUS ABB=ON L10 AND (L5 OR ?PREDNISONE? OR
?PREDNISOLONE? OR ?CYCLOSPORINE? OR ?METHOTREXAT? OR ?ANTI? (W) ?
LYMPHOCYTE? (W) ?GLOBULIN? OR ?ANTI? (W) T(W) ?CELL? (W) (MONOCLONAL? (W) ?ANTIBOD? OR ?IMMUNOTOXIN?))
.L13     26 SEA FILE=HCAPLUS ABB=ON L11 OR L12
.L17     15 SEA FILE=USPATFULL ABB=ON L13 AND (PRD<20010813 OR PD<20010813
)
```

=> d ibib abs 117 1-15

L17 ANSWER 1 OF 15 USPATFULL on STN
ACCESSION NUMBER: 2005:137498 USPATFULL
TITLE: Cellular compositions which facilitate engraftment of hematopoietic stem cells while minimizing the risk of **gvhd**
INVENTOR(S): Ildstad, Suzanne T, Louisville, KY, UNITED STATES

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2005118142	A1	20050602
APPLICATION INFO.:	US 2003-485842	A1	20020801 (10)
	WO 2002-US24402		20020801

	NUMBER	DATE	
PRIORITY INFORMATION:	US 2003-60309243	20010801	<--
DOCUMENT TYPE:	Utility		
FILE SEGMENT:	APPLICATION		
LEGAL REPRESENTATIVE:	FROST BROWN TODD, LLC, 2200 PNC CENTER, 201 E. FIFTH STREET, CINCINNATI, OH, 45202, US		
NUMBER OF CLAIMS:	36		
EXEMPLARY CLAIM:	1		
NUMBER OF DRAWINGS:	8 Drawing Page(s)		
LINE COUNT:	2126		

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The present invention provides for cellular compositions which facilitate engraftment of hematopoietic stem cells from a syngeneic, allogeneic or xenogeneic donor. The cellular compositions of the invention facilitate engraftment while minimizing the risk of graft versus host disease in the graft recipient. According to a preferred embodiment of the invention, a cell composition is provided, which cell composition comprises hematopoietic stem cells, such as CD34.sup.+ cells and/or facilitating cells, in combination with $\alpha\beta$ TCR.sup.+ T cells. The invention also relates to methods of using the cellular compositions of the invention to induce donor specific tolerance in a recipient, thus allowing the transplantation of donor organs, cells and tissues. Also disclosed are methods of treating leukemia and

cancer as well as infectious diseases caused by viruses.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L17 ANSWER 2 OF 15 USPATFULL on STN

ACCESSION NUMBER:

2004:313909 USPATFULL

TITLE:

Mixed chimerism and tolerance

INVENTOR(S):

Sykes, Megan, Charlestown, MA, UNITED STATES

PATENT ASSIGNEE(S):

The General Hospital Corporation, a Massachusetts corporation (U.S. corporation)

NUMBER	KIND	DATE
--------	------	------

PATENT INFORMATION:

US 2004247579 A1 20041209

US 6877514 B2 20050412

APPLICATION INFO.:

US 2003-696127 A1 20031029 (10)

RELATED APPLN. INFO.:

Division of Ser. No. US 2002-155878, filed on 24 May 2002, GRANTED, Pat. No. US 6718986 Division of Ser. No. US 1999-374498, filed on 13 Aug 1999, GRANTED, Pat. No. US 6412492 Division of Ser. No. US 1997-855705, filed on 8 May 1997, GRANTED, Pat. No. US 6006752

NUMBER	DATE
--------	------

PRIORITY INFORMATION:

US 1996-17099P 19960509 (60)

<--

DOCUMENT TYPE:

Utility

FILE SEGMENT:

APPLICATION

LEGAL REPRESENTATIVE:

FISH & RICHARDSON PC, 225 FRANKLIN ST, BOSTON, MA, 02110

NUMBER OF CLAIMS:

11

EXEMPLARY CLAIM:

1

NUMBER OF DRAWINGS:

8 Drawing Page(s)

LINE COUNT:

1916

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB A method of inducing tolerance without whole body irradiation.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L17 ANSWER 3 OF 15 USPATFULL on STN

ACCESSION NUMBER:

2004:150954 USPATFULL

TITLE:

Methods for treating disorders of neuronal deficiency with bone marrow-derived cells

INVENTOR(S):

Blau, Helen M., Menlo Park, CA, UNITED STATES

Brazelton, Timothy, Cupertino, CA, UNITED STATES

Weimann, James M., Palo Alto, CA, UNITED STATES

PATENT ASSIGNEE(S):

The Board of Trustees of the Leland, Palo Alto, CA (U.S. corporation)

NUMBER	KIND	DATE
--------	------	------

PATENT INFORMATION:

US 2004115175 A1 20040617

APPLICATION INFO.:

US 2003-688747 A1 20031016 (10)

RELATED APPLN. INFO.:

Continuation-in-part of Ser. No. US 2001-993045, filed on 13 Nov 2001, PENDING

NUMBER	DATE
--------	------

PRIORITY INFORMATION:

US 2000-247128P 20001110 (60)

<--

DOCUMENT TYPE:

Utility

FILE SEGMENT: APPLICATION
 ·LEGAL REPRESENTATIVE: ROPES & GRAY LLP, ONE INTERNATIONAL PLACE, BOSTON, MA,
 02110-2624
 NUMBER OF CLAIMS: 40
 EXEMPLARY CLAIM: 1
 NUMBER OF DRAWINGS: 11 Drawing Page(s)
 LINE COUNT: 2455

AB The invention provides, among other things, novel methods of treating neurological disorders which result in the loss of neurons (neuronal deficiencies). Bone marrow-derived cells are administered to individuals suffering from neuronal deficiencies. Administration of bone marrow-derived cells results in formation of bone marrow derived neurons, whether formed de novo or as a result of fusion with an existing neuron, thereby replacing or repairing lost or damaged neurons. The methods of the invention may also be used for memory augmentation in memory impaired individuals.

L17 ANSWER 4 OF 15 USPATFULL on STN
 ACCESSION NUMBER: 2004:88251 USPATFULL
 TITLE: Blockade of T cell migration into epithelial GVHD target tissues as an approach to achieving anti-tumor effects against lymphohematopoietic malignancies without GVHD
 INVENTOR(S): Sykes, Megan, Charlestown, MA, UNITED STATES
 PATENT ASSIGNEE(S): The General Hospital Corporation, Boston, MA, 02110 (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2004067220	A1	20040408
APPLICATION INFO.:	US 2003-437707	A1	20030514 (10)
RELATED APPLN. INFO.:	Continuation of Ser. No. WO 2001-US43797, filed on 14 Nov 2001, PENDING		

	NUMBER	DATE	
PRIORITY INFORMATION:	US 2000-248332P	20001114 (60)	<--
DOCUMENT TYPE:	Utility		
FILE SEGMENT:	APPLICATION		
LEGAL REPRESENTATIVE:	HALE AND DORR, LLP, 60 STATE STREET, BOSTON, MA, 02109		
NUMBER OF CLAIMS:	64		
EXEMPLARY CLAIM:	1		
NUMBER OF DRAWINGS:	3 Drawing Page(s)		
LINE COUNT:	2079		

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Antagonists of T cell migration are used to reduce GVHD in recipients of hematopoietic cell grafts. The administration of antagonists of T cell migration can be used in combination with conventional methods of bone marrow transplantation and in combination with the administration of donor leukocytes.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L17 ANSWER 5 OF 15 USPATFULL on STN
 ACCESSION NUMBER: 2003:225266 USPATFULL
 TITLE: Treatment of hematologic disorders
 INVENTOR(S): Sykes, Megan, Boston, MA, UNITED STATES
 Spitzer, Thomas R., Andover, MA, UNITED STATES

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2003157077	A1	20030821
APPLICATION INFO.:	US 2003-374302	A1	20030225 (10)
RELATED APPLN. INFO.:	Continuation of Ser. No. US 1998-191970, filed on 13 Nov 1998, GRANTED, Pat. No. US 6558662		

	NUMBER	DATE
PRIORITY INFORMATION:	US 1997-73230P	19971114 (60)
DOCUMENT TYPE:	Utility	<--
FILE SEGMENT:	APPLICATION	
LEGAL REPRESENTATIVE:	ROPES & GRAY LLP, ONE INTERNATIONAL PLACE, BOSTON, MA, 02110-2624	
NUMBER OF CLAIMS:	36	
EXEMPLARY CLAIM:	1	
NUMBER OF DRAWINGS:	2 Drawing Page(s)	
LINE COUNT:	2151	

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The inventors have discovered that hematologic disorders, e.g., both neoplastic (hematologic **cancers**) and non-neoplastic conditions, can be treated by the induction of mixed chimerism using myeloreductive, but not myeloablative, conditioning. Methods of the invention reduce **GVHD**, especially **GVHD** associated with mismatched allogeneic or xenogeneic donor tissue, yet provide, for example, significant graft-versus-leukemia (GVL) effect and the like.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L17 ANSWER 6 OF 15 USPATFULL on STN
 ACCESSION NUMBER: 2003:123081 USPATFULL
 TITLE: Transgenic swine & swine cells having human HLA genes
 INVENTOR(S): Seebach, Joerg, Boston, MA, United States
 Sachs, David H., Newton, MA, United States
 DerSimonian, Harout, Wellesley, MA, United States
 LeGuern, Christian, Newton, MA, United States
 PATENT ASSIGNEE(S): The General Hospital Corporation, Boston, MA, United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 6558663	B1	20030506
APPLICATION INFO.:	US 1999-457177		19991208 (9)
RELATED APPLN. INFO.:	Division of Ser. No. US 1996-692843, filed on 2 Aug 1996, now patented, Pat. No. US 6030833		

	NUMBER	DATE
PRIORITY INFORMATION:	US 1995-1900P	19950804 (60)
DOCUMENT TYPE:	Utility	<--
FILE SEGMENT:	GRANTED	
PRIMARY EXAMINER:	Wehbe', Anne M.	
LEGAL REPRESENTATIVE:	Fish & Richardson P.C.	
NUMBER OF CLAIMS:	16	
EXEMPLARY CLAIM:	1	
NUMBER OF DRAWINGS:	3 Drawing Figure(s); 1 Drawing Page(s)	
LINE COUNT:	2834	

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Methods of promoting tolerance and inhibiting NK cell mediated attack in a human recipient to a swine graft are disclosed. The methods include introducing into the recipient a swine hematopoietic stem cell which has been transformed with a transgene encoding a human MHC class I protein that inhibits recipient NK cell mediated attack.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L17 ANSWER 7 OF 15 USPATFULL on STN

ACCESSION NUMBER: 2003:110472 USPATFULL
 TITLE: Mixed chimerism and tolerance
 INVENTOR(S): Sykes, Megan, Charlestown, MA, UNITED STATES
 PATENT ASSIGNEE(S): The General Hospital Corporation, Boston, MA, UNITED STATES, 02110 (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2003075187	A1	20030424
	US 6718986	B2	20040413
APPLICATION INFO.:	US 2002-155878	A1	20020524 (10)
RELATED APPLN. INFO.:	Division of Ser. No. US 1999-374498, filed on 13 Aug 1999, GRANTED, Pat. No. US 6412492 Division of Ser. No. US 1997-855705, filed on 8 May 1997, GRANTED, Pat. No. US 6006752		

	NUMBER	DATE
PRIORITY INFORMATION:	US 1996-17099P	19960509 (60) <--
DOCUMENT TYPE:	Utility	
FILE SEGMENT:	APPLICATION	
LEGAL REPRESENTATIVE:	HALE AND DORR, LLP, 60 STATE STREET, BOSTON, MA, 02109	
NUMBER OF CLAIMS:	26	
EXEMPLARY CLAIM:	1	
NUMBER OF DRAWINGS:	8 Drawing Page(s)	
LINE COUNT:	1953	

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB A method of inducing tolerance without whole body irradiation.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L17 ANSWER 8 OF 15 USPATFULL on STN

ACCESSION NUMBER: 2002:300807 USPATFULL
 TITLE: Methods for treating disorders of neuronal deficiency with bone marrow-derived cells
 INVENTOR(S): Brazelton, Timothy R., Cupertino, CA, UNITED STATES
 Blau, Helen M., Menlo Park, CA, UNITED STATES

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2002168350	A1	20021114
APPLICATION INFO.:	US 2001-993045	A1	20011113 (9)

	NUMBER	DATE
PRIORITY INFORMATION:	US 2000-247128P	20001110 (60) <--
DOCUMENT TYPE:	Utility	
FILE SEGMENT:	APPLICATION	
LEGAL REPRESENTATIVE:	MORRISON & FOERSTER LLP, 755 PAGE MILL RD, PALO ALTO, CA, 94304-1018	

NUMBER OF CLAIMS: 34
 EXEMPLARY CLAIM: 1
 LINE COUNT: 1696

AB The invention provides novel methods of treating neurological disorders which result in the loss of neurons (neuronal deficiencies). Bone marrow-derived cells are administered to individuals suffering from neuronal deficiencies. Administration of bone marrow-derived cells results in formation of new neurons in the nervous system, thereby replacing lost neurons. The methods of the invention may also be used for memory augmentation in memory impaired individuals.

L17 ANSWER 9 OF 15 USPATFULL on STN
 ACCESSION NUMBER: 2002:159528 USPATFULL
 TITLE: Mixed chimerism and tolerance
 INVENTOR(S): Sykes, Megan, Boston, MA, United States
 PATENT ASSIGNEE(S): The General Hospital Corporation, Boston, MA, United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 6412492	B1	20020702
APPLICATION INFO.:	US 1999-374498		19990813 (9)
RELATED APPLN. INFO.:	Division of Ser. No. US 1997-855705, filed on 8 May 1997, now patented, Pat. No. US 6006752		

	NUMBER	DATE
PRIORITY INFORMATION:	US 1996-17099P	19960509 (60) <--
DOCUMENT TYPE:	Utility	
FILE SEGMENT:	GRANTED	
PRIMARY EXAMINER:	Isabella, David J.	
LEGAL REPRESENTATIVE:	Hale and Dorr LLP	
NUMBER OF CLAIMS:	31	
EXEMPLARY CLAIM:	1	
NUMBER OF DRAWINGS:	13 Drawing Figure(s); 8 Drawing Page(s)	
LINE COUNT:	1977	

AB A method of inducing tolerance without whole body irradiation.

L17 ANSWER 10 OF 15 USPATFULL on STN
 ACCESSION NUMBER: 2001:223705 USPATFULL
 TITLE: TREATMENT OF HEMATOLOGIC DISORDERS
 INVENTOR(S): SYKES, MEGAN, BOSTON, MA, United States
 PATENT ASSIGNEE(S): SPITZER, THOMAS R., ANDOVER, MA, United States
 The General Hospital Corporation (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2001048921	A1	20011206
	US 6558662	B2	20030506
APPLICATION INFO.:	US 1998-191970	A1	19981113 (9)

	NUMBER	DATE
PRIORITY INFORMATION:	US 1997-73230P	19971114 (60) <--
DOCUMENT TYPE:	Utility	
FILE SEGMENT:	APPLICATION	
LEGAL REPRESENTATIVE:	FOLEY, HOAG & ELIOT, LLP, PATENT GROUP, ONE POST OFFICE	

SQUARE, BOSTON, MA, 02109

NUMBER OF CLAIMS: 36
 EXEMPLARY CLAIM: 1
 NUMBER OF DRAWINGS: 2 Drawing Page(s)
 LINE COUNT: 2152

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The inventors have discovered that hematologic disorders, e.g., both neoplastic (hematologic **cancers**) and non-neoplastic conditions, can be treated by the induction of mixed chimerism using myeloreductive, but not myeloablative, conditioning. Methods of the invention reduce **GVHD**, especially **GVHD** associated with mismatched allogeneic or xenogeneic donor tissue, yet provide, for example, significant graft-versus-leukemia (GVL) effect and the like.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L17 ANSWER 11 OF 15 USPATFULL on STN

ACCESSION NUMBER: 2001:194150 USPATFULL
 TITLE: L-leucyl-L-leucine methyl ester treatment of donor lymphocyte infusions in bone marrow transplant patients
 INVENTOR(S): Korngold, Robert, Cherry Hill, NJ, United States
 Flomenberg, Neal, Cherry Hill, NJ, United States
 Hsieh, Michael, Philadelphia, PA, United States

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2001036664	A1	20011101
APPLICATION INFO.:	US 2001-803223	A1	20010309 (9)

	NUMBER	DATE	
PRIORITY INFORMATION:	US 2000-188391P	20000310 (60)	<--
DOCUMENT TYPE:	Utility		
FILE SEGMENT:	APPLICATION		
LEGAL REPRESENTATIVE:	THOMAS JEFFERSON UNIVERSITY, INTELLECTUAL PROPERTY DIVISION, 1020 WALNUT STREET, SUITE 620, PHILADELPHIA, PA, 19107		
NUMBER OF CLAIMS:	5		
EXEMPLARY CLAIM:	1		
NUMBER OF DRAWINGS:	2 Drawing Page(s)		
LINE COUNT:	413		

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The present invention relates to a method of inhibiting graft-versus-host disease in allogeneic **hematopoietic stem cell transplant** (HSCT) patients by using L-leucyl-L-leucine methyl ester (LLME) to eliminate selective cytotoxic T cells in donor lymphocyte infusions (DLI). LLME has been shown to inhibit **GVHD** in animal models by selectively inducing apoptosis in natural killer cells and cytotoxic T cells. The application of LLME to the human clinical HSCT situation, however, has been hampered by HSC toxicity when unseparated marrow is treated at the concentrations necessary to purge **GVHD**-inducing T cells prior to infusion. In the present invention, this problem is circumvented by the LLME ex vivo treatment of DLI administered following transplantation of T cell-depleted HSC. In this setting, the effects of LLME on HSC contained within the DLI are irrelevant for clinical outcome. In another embodiment, the risk of toxicity to the stem cell population is avoided by ex vivo LLME treatment of donor lymphocytes after separation of CD34.sup.+ stem cells and then co-administration of the LLME-treated

donor CD34.sup.- fraction and the untreated CD34.sup.+ stem cells.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L17 ANSWER 12 OF 15 USPATFULL on STN
 ACCESSION NUMBER: 2000:24507 USPATFULL
 TITLE: Transgenic swine and swine cells having human HLA genes
 INVENTOR(S): Seebach, Joerg, Boston, MA, United States
 Sachs, David H., Newton, MA, United States
 DerSimonian, Harout, Wellesley, MA, United States
 LeGuern, Christian, Newton, MA, United States
 PATENT ASSIGNEE(S): The General Hospital, MA, United States (U.S.
 corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 6030833		20000229
APPLICATION INFO.:	US 1996-692843		19960802 (8) <--

	NUMBER	DATE
PRIORITY INFORMATION:	US 1995-1900P	19950804 (60) <--
DOCUMENT TYPE:	Utility	
FILE SEGMENT:	Granted	
PRIMARY EXAMINER:	Saunders, David	
ASSISTANT EXAMINER:	VanderVegt, F. Pierre	
LEGAL REPRESENTATIVE:	Fish & Richardson P.C.	
NUMBER OF CLAIMS:	14	
EXEMPLARY CLAIM:	1	
NUMBER OF DRAWINGS:	3 Drawing Figure(s); 1 Drawing Page(s)	
LINE COUNT:	2801	

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB A genetically engineered swine cell having a transgene encoding a human HLA protein.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L17 ANSWER 13 OF 15 USPATFULL on STN
 ACCESSION NUMBER: 1999:169148 USPATFULL
 TITLE: Mixed chimerism and tolerance
 INVENTOR(S): Sykes, Megan, Boston, MA, United States
 PATENT ASSIGNEE(S): The General Hospital Corporation, Boston, MA, United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 6006752		19991228
APPLICATION INFO.:	US 1997-855705		19970508 (8) <--

	NUMBER	DATE
PRIORITY INFORMATION:	US 1996-17099P	19960509 (60) <--
DOCUMENT TYPE:	Utility	
FILE SEGMENT:	Granted	
PRIMARY EXAMINER:	Isabella, David J.	
LEGAL REPRESENTATIVE:	Fish & Richardson P.C.	
NUMBER OF CLAIMS:	53	
EXEMPLARY CLAIM:	1	
NUMBER OF DRAWINGS:	5 Drawing Figure(s); 5 Drawing Page(s)	

LINE COUNT: 2116

AB A method of inducing tolerance without whole body irradiation.

L17 ANSWER 14 OF 15 USPATFULL on STN

ACCESSION NUMBER: 1998:150448 USPATFULL

TITLE:

INVENTOR(S): Sachs, David H., Newton, MA, United States

Arn, J. Scott, North Andover, MA, United States

Lorf, Thomas, Hardegsen/Gladebeck, Germany, Federal
Republic ofPATENT ASSIGNEE(S): The General Hospital Corporation, Boston, MA, United
States (U.S. corporation)

NUMBER KIND DATE

PATENT INFORMATION: US 5843425 19981201 <--

APPLICATION INFO.: US 1995-461693 19950605 (8)

RELATED APPLN. INFO.: Continuation-in-part of Ser. No. US 1994-266427, filed
on 19 Jun 1994, now patented, Pat. No. US 5614182 Ser.
No. Ser. No. US 1992-838595, filed on 19 Feb 1992, now
abandoned Ser. No. Ser. No. US 1995-451210, filed on 26
May 1995, now abandoned Ser. No. Ser. No. US
1994-220371, filed on 29 Mar 1994, now abandoned Ser.
No. Ser. No. US 1995-458720, filed on 1 Jun 1995 Ser.
No. Ser. No. US 1994-243653, filed on 16 May 1994, now
patented, Pat. No. US 5658564 Ser. No. Ser. No. US
1993-114072, filed on 30 Aug 1993, now patented, Pat.
No. US 5624823 Ser. No. Ser. No. US 1993-150739, filed
on 19 Nov 1993, now abandoned And Ser. No. US
1994-212228, filed on 14 Mar 1994, now abandoned , said
Ser. No. US -451210 which is a continuation of Ser.
No. US -838595

DOCUMENT TYPE: Utility

FILE SEGMENT: Granted

PRIMARY EXAMINER: Chambers, Jasemine C.

ASSISTANT EXAMINER: Hauda, Karen M.

LEGAL REPRESENTATIVE: Louis Meyers, Lahive & Cockfield

NUMBER OF CLAIMS: 19

EXEMPLARY CLAIM: 1,3,5

LINE COUNT: 1579

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB A method of preparing swine donor tissue which includes hematopoietic
stem cells and T cells for transplantation into a recipient mammal other
than a swine. The method includes the swine donor tissue with an
antibody which binds the epitope recognized by the mAb 2-6-15 monoclonal
antibody. The binding facilitates depletion of T cells about as
efficiently or more efficiently than does the mAb 2-6-15 monoclonal
antibody and results in about the same or less depletion of stem cells
as does the mAb 2-6-15 monoclonal antibody.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L17 ANSWER 15 OF 15 USPATFULL on STN

ACCESSION NUMBER: 97:36084 USPATFULL

TITLE: DNA encoding porcine interleukin-10

INVENTOR(S): Sachs, David H., Newton, MA, United States

Leguern, Christian A., Newton, MA, United States

Sykes, Megan, Charlestown, MA, United States

PATENT ASSIGNEE(S) : Blancho, Gilles JF., Cambridge, MA, United States
The General Hospital Corporation, Boston, MA, United States (U.S. corporation)

PATENT INFORMATION:	NUMBER	KIND	DATE
	US 5624823		19970429 <--
APPLICATION INFO.:	US 1993-114072		19930830 (8)
RELATED APPLN. INFO. :	Continuation-in-part of Ser. No. US 1991-797555, filed on 22 Nov 1991, now abandoned And a continuation-in-part of Ser. No. US 1992-838595, filed on 19 Feb 1992, now abandoned And a continuation-in-part of Ser. No. US 1993-63171, filed on 17 May 1993, now abandoned And a continuation-in-part of Ser. No. US 1993-62946, filed on 17 May 1993, now abandoned , said Ser. No. US -838595 which is a continuation-in-part of Ser. No. US 1992-817761, filed on 8 Jan 1992, now abandoned , said Ser. No. US -63171 which is a continuation-in-part of Ser. No. US -838595 And Ser. No. US -797555 , said Ser. No. US -62946 which is a continuation-in-part of Ser. No. US -838595		

DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Walsh, Stephen G.
ASSISTANT EXAMINER: Kemmerer, Elizabeth C.
LEGAL REPRESENTATIVE: Myers, Ph.D., LouisLahive & Cockfield
NUMBER OF CLAIMS: 27
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 3 Drawing Figure(s); 3 Drawing Page(s)
LINE COUNT: 1826
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Purified DNA encoding porcine IL-10, porcine IL-10, and methods of inducing immunological tolerance and inhibiting graft versus host disease.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.